ESTIMATING BURULI ULCER PREVALENCE IN SOUTHWESTERN GHANA

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Mycobacterium ulcerans is sweeping across sub-Saharan Africa, but little is known about the mode of transmission and its natural reservoirs. Since the only effective treatment is excision of the infection and surrounding tissue, early diagnosis and treatment is the only way to reduce the havoc associated with Buruli ulcer. Using data from a national case search survey conducted in Ghana during 2000 and suspected risk factors this study tests the hypothesized factors and probes the challenges of developing a spatial epidemiological regression model to explain Buruli ulcer prevalence in the southwestern region of Ghana representing 42 districts. Results suggest that prevalence is directly related to the degree of land cover classified as soil, elevation differential, and percent rural population of the area.

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CHAPTER 1

INTRODUCTION

Buruli ulcer (BU) has become a major public health concern in African countries today. It is the third most common form of mycobacterium infection in healthy people, following just behind tuberculosis and leprosy, and is the most poorly understood of these three diseases (WHO, 2005). Very little is known about this disease which destroys the skin, muscle, bone structures and ultimately, if left untreated, can cause death. Even with treatment, deformities can and do occur. The only effective treatment is surgery where the infection and the area surrounding it are removed. The effects of Buruli ulcer on a person, even after treatment, range from lesions, deformities, amputation, to loss of limb use. Buruli ulcer is endemic in more than thirty countries and affects thousands of people every year. About 70% of all cases involve children (WHO, 2005). Little is known about how it is transmitted. To deal with this emerging global threat, the World Health Organization (WHO) established the Global Buruli Ulcer Initiative in 1998 (Amofa et al., 2002).

Though many factors about Buruli ulcer remain unknown, current research suggests several factors associated with the prevalence of the disease. For example, living in close proximity to slow moving water such as swamps, man made lakes, dams, and creeks, or living in lower elevation areas appear to have a higher risk for Buruli ulcer (Duker et al., 2004). Similarly, living in areas with marshland vegetation or areas that have a high degree of human impact on the landscape such as construction of small scale mining, roads, hydropower dams, and new settlements appears to carry a higher risk of disease. Finally, males appear to have a slightly higher risk. This study will explore a multiple regression model using some of these hypothesized risk factors. The result will be a model for estimating prevalence of Buruli ulcer in selected places and regions.

Significance of the Thesis

This thesis has two main goals. First, it will examine the geography of Buruli Ulcer (BU) in southwestern Ghana and the variables that are associated with areas that have high rates of BU. Second, using simple multivariate statistics, and Geographic Information Systems (GIS), it will probe for statistical significance between BU rates and selected hypothesized variables. This may lead to a model for estimating the spatial pattern of BU prevalence in the study area. If such a model were available, health workers would be able to target education and surveillance activities to areas where Buruli Ulcer is underreported. This study will explore the prospects of developing a model for estimating BU prevalence.

Such a model is critical for several reasons. With seventy percent of the cases of Buruli ulcer being found in children under the age of 15, and the definitive form of treatment being the removal of the infected area and surrounding tissue, early detection is imperative (Asiedu et al., 2000). Furthermore, without treatment (and sometimes even with treatment) lifelong disfigurement can and does occur. Such physical impairment introduces permanent social problems. What is also of interest is the fact that there is consensus that the cases of Buruli ulcer are under reported; the severity of the problem maybe much greater than the community realizes. Consequentially this research seeks to examine which of the many factors hypothesized to be associated with BU show significant relations with BU in Ghana. It will also examine the feasibility of testing these hypotheses using currently available geographic tools and data. Particularly the potential of GIS for geographic analysis of disease, beyond mere visualization, to produce pretty maps of disease, will be examined. By integrating different contributing variables to demonstrate the layered context of disease and the interactions among multiple variables in the geography of disease, GIS analysis can provide rare insights into the spatial patterns of diseases and hypothesized causation.

Research Questions

1) What is the spatial pattern of BU in southwestern Ghana?

2) How do the hypothesized factors that influence Buruli ulcer relate to the spatial pattern of prevalence of the disease in an endemic district in Ghana?

3) What are the challenges of developing a spatial epidemiological regression model to explain the spatial pattern of BU prevalence?

CHAPTER 2

REVIEW OF LITERATURE

Background

After tuberculosis and leprosy, Buruli ulcer is the third most common mycobacterial infection (Asiedu et al., 2000). *Mycobacteria ulcerans*, which causes Buruli ulcer, is a slow-growing mycobacterium that classically infects the skin and subcutaneous tissues, giving rise to indolent (painless) ulcers. *M. ulcerans* grows optimally at a temperature of 90^{o}F (32°C) in the tropical and sub-tropical zones on earth (WHO, 2005). The name Buruli ulcer comes from the district of Buruli in Uganda where the first large number of cases appeared in the 1960s and early 1970s. In Australia the disease is also called Barinsdal disease.

The history of Buruli ulcer can be divided into two different periods – pre and post 1980. Sir Albert Cook (1897), the first physician to practice in Uganda, described two patients with necrotizing skin ulceration during the first year of his work at Mengo Hospital (Lunn et al., 1965). The cases, however, were not published in medical literature. In 1948 Dr. Peter MacCallum and his colleagues, Tolhurst, Buckle and Sission from Australia, gave “the first account of clinical, pathological, bacteriological, and experimental aspects of Buruli ulcer, a new mycobacterial infection that was subsequently named *Mycobacterium ulcerans*” (WHO, 2005). In the 1960s through the 1970s, the number of cases reported exploded in Uganda, the Democratic Republic of the Congo, Papua New Guinea and other countries, giving rise to a new epidemic in the developing world (Asiedu et al., 2000).

Since the 1980s, Buruli ulcer has emerged as a serious public health threat with ever increasing numbers. West African countries are the hardest hit and the number of countries affected is growing rapidly. Three main events have happened since 1980. First, in December 1997, on the occasion of his visit to Côte d'Ivoire, Dr Hiroshi Nakajima, then Director-General of the World Health Organization (WHO), announced that WHO "would take the lead to mobilize the world's expertise and resources to fight Buruli ulcer as a serious public health problem" (WHO, 2005). Second, in 1998, the World Health Organization launched "the Global Buruli Ulcer Initiative (GBUI) to coordinate control and research efforts, and organized the first International Conference on Buruli ulcer control and research" (WHO, 2005). The third and final event occurred in May 2004 the World Health Assembly adopted a resolution on Buruli ulcer which called for "increasing surveillance, control and intensified research to develop tools to diagnose, treat and prevent the disease" (WHO, 2005).

The etiology of Buruli ulcer is unknown at this time but overwhelming evidence points to an environmental source (Asiedu et al., 2000). Buruli ulcer is caused by *Mycobacteria ulcerans* which is an acid-fast bacilli that releases a toxin into the tissue. Once released, it destroys the surrounding tissue while at the same time suppressing the immune system.

Although Buruli ulcer is potentially transmittable between humans or animals, such transmission has not been confirmed. (Asiedu et al., 2000). But a recent case of Buruli ulcer reported in a 13 year old girl living in Benin occurred after a human bite (Debacker, Zinsou, Aguia, et al., 2003). The infection occurred within thirty days after the girl was bitten by a fellow classmate and appeared in the same location as the bite.

While this is the first reported case of Buruli ulcer showing up after a human bite researchers are still unsure if the infection occurred because of the playmate. Researchers hypothesized that the playmates mouth could have been contaminated or trauma activated a latent focus of *m. ulcerans* on the skin of the girl or the trauma was in a location that allowed the etiological agent access into the girls body (Debacker et al., 2003).

Mycobacterium ulcerans manifests in four strains of Buruli ulcer: African, Australian, Asian, and American, with the African strain being the most virulent. Like the etiology, the reservoir of *M. ulcerans* is unknown but has been suspected to be associated with certain plants in swampy areas. Studies in Uganda associated cases with certain grasses and sage: for example, *Hyperrhenia*, *Imperata cylindrical*, and *Panicum maxium* (Barker, Clancey, & and Rao 1972). A direct link was confirmed with grasses and sage and high Buruli ulcer prevalence. Other hypothesized reservoirs for Buruli ulcer are insects, fish, cattle, and other livestock (Asiedu et al., 2000). The specific mode of transmission is not known, but the disease predominately occurs in slow-moving to stagnant water such as swamps, lakes, ponds, and slow-moving streams. Environmental organisms are suspected to be the mode of transmission, such as the aquatic insects *Naucoris* and *Dyplonychus* species and the *Aplocheilichthys* fish. Trauma is suspected as the way in which the disease normally enters the system. Hypothesized examples include hypodermic needle puncture, severe gunshot wound or exploding mine.

Current research suggests that Buruli ulcer is not transmitted from patient to patient, but researchers caution against this dismissal of person-to-person transmission

(Asiedu et al., 2000). A study in Benin found that 10 out of 28 patients had relatives who were also infected with the disease (Muelder & Nourou, 1990). Radford (1974) reported a case which developed in hospital in a child accompanying its mother who had been treated for the condition for 2 months, and a similar case that occurred between siblings in a hospital in Malaya (Radford, 1974).

Once the disease is introduced into the skin tissue, the organism releases toxins that multiply within the fat cells. In the early phase of infection very little immune response occurs and a burulin skin test is negative. During this stage the toxin may be neutralized or the organism may cease to exist or produce a toxin in the infected area. If this does not occur healing begins when the host develops immunity, at which time the burulin skin test may become positive (Portaels, Johnson, & Meyers, 2001). During this time the cells destroy the etiological agent (*M. ulcerans*) and the disease subsides with scarring. At this stage bones may also be affected by direct spread from the lesion or as a result of *M. ulcerans* bacteraemia (Portaels et al., 2001).

Buruli ulcer incubation is 2 to 3 months with an unknown latency period; it is suspected, however, to be many years (Portaels et al., 2001). There are three main stages of Buruli ulcer: the non-ulcerative (Figure 1), ulcerative (Figure 2), and post-ulcerative (sequelae) (Figure 3). In the non-ulcerative stage the disease manifests as a painless spot on the epidermis of the body and can be easily treated. At this stage Buruli ulcer manifests as a papule, nodule, plaque, or edematous with the nodule form prominent in West Africa. Treatment at this stage is the removal of the nodule and the surrounding tissue. Cost of this treatment is usually less than $30 and can be done in a matter of hours with minimal scarring (Asiedu et al., 2000). If left untreated, however,

Figure 1: Non-ulcerative.

Source: World Health Organization, 2006.

Figure 2: Ulcerative.

Source: World Health Organization, 2006.

Figure 3: Post-ulcerative.

Source: World Health Organization, 2006.

the disease progresses to the ulcerative stage with painless lesion, characterized by a necrotic center, undermined edges and edematous skin. It is the absence of super-infections that enable the ulcers to be painless or minimally painful. After the ulcerative stage, comes the post-ulcerative (sequelae) which ushers in complications resulting directly from the infection such as, contracture deformities, loss of sight and amputation.

Diagnosis of Buruli ulcer can be accomplished in three ways: clinically or through the use of a laboratory or radiology test (Portaels et al., 2001). Clinical diagnosis is based on four criteria when conducted by an experienced person in the field: (a) patient lives in or has traveled to a known endemic area; (b) most patients are children under 15 years of age; (c) about 85% of lesions are on the limbs; and (d) lower limb lesions are twice as common as upper limb lesions. Laboratory diagnosis requires two of the following to be positive: acid-face bacilli in a smear stained by the Ziehl-Neelsen (ZN) technique, positive culture of *M. ulcerans* (but this requires 6-8 weeks or longer), histopathological study of excisional biopsy specimen (result available rapidly), and positive polymerase chain reaction (PCR) for DNA from *M. ulcerans*. Radiological diagnosis is increasingly used in West Africa because osteomyelitis has become increasingly more common (Portaels et al., 2001). While the diagnostic method used depends on the location of the patient, access to health care workers and medical facilities, and the technology available, typically diagnostic methods to confirm *M. ulcerans* infection are expensive and ill-suited to low resource areas (Raghunathan, Whitney, Asamoa, et al., 2005).

Treatment for Buruli ulcer is conducted in several ways depending on what is available and considered most effective in the area. Five major treatment methods, with varying degrees of effectiveness are currently available: (a) the use of drugs, (b) surgery, (c) heat, (d) hyperbaric oxygen, and (e) traditional medicine. Surgery, the only definitive form of treatment, involves the excision of the infection and surrounding tissue. Early treatment is imperative for a successful result. Hyperbaric oxygen and heat have been shown to be effective in developed countries, but because of limited access to technology in endemic areas they are not practical. Drug treatment has also shown some effectiveness, but only at the earliest stages of infection. Finally, there has been some promising work with traditional medicine, but often the treatment course is long and damage to the body has already occurred. Major complications of the disease range from contracture and bleeding to secondary infection, disfigurement and death (WHO, 2005).

The prognosis varies greatly depending on when the disease is caught. If detected early there is a minimal recovery period and little scarring. But, if late detection occurs the victims are often faced with deformities, amputation, and sometimes death. The final major problem with Buruli ulcer is that there is a 30% reoccurrence rate (WHO, 2005).

Medical Geography Factors

There are many unknowns about Buruli ulcer and the definitive factors that directly affect the prevalence rate. Several variables have been hypothesized ranging from age to environmental factors. Age is important to note, since 70% of all cases occur in children under 15 (WHO, 2005). The youngest reported case to date is a 6-week old baby; the oldest is 70 years of age (Radford, 1974). Population structure is important in Buruli ulcer because in many countries where Buruli ulcer is endemic, 50% or more of the population is under the age of 18 (Asiedu et al., 2000).

Gender plays a part in Buruli ulcer, not necessarily because of a specific difference of genetics, but more than likely because of occupation roles such as farming for men, bathing of children, and the method in which women do laundry (Debacker et al., 2005). Most studies have shown slightly higher incidences among males than females. A case control study by Debacker, Aguiar, Steunou, Zinsou, Meyers, Scott, Dramaix and Portaels found that males and people of the ages of 59+ had a higher risk of Buruli ulcer infection than the average person (Debacker et al., 2004).

Several environmental factors are hypothesized to be associated with increased risk of Buruli ulcer. Prominent among these are proximity to water source, activities involving water sources, and environmental modification. Proximity to water bodies is the most frequently cited environmental factor. Research suggests that swamps, slow-moving streams, stagnant water, and artificial lakes all bring an increased risk of transmission (WHO, 2005). A case control study by Reghunathan, Asamoa, and Taylor in Ghana showed people living less than 5 minutes walking time from a primary drinking source had twice the risk of being infected with Buruli ulcer. Similarly, people with a walking time to laundry water source of less than 7 minutes were twice as likely to have been infected with Buruli ulcer. The second part of the study found that people who waded in rivers or steams were almost 3 times more likely to be infected with Buruli ulcer. Finally, the study found that people who bathed in water of an open borehole were 2.6 times more likely to be infected (Reghunathan, Asamoa, & Taylor, 2005).

The second environmental factor that increases a person's risk is activities involving water sources such as bathing, laundry, swimming and others. Increased interaction with the suspected mode of transmission brings on risk increases. A case control study, conducted in the Daloa Region of Cote D'Ivoire, found that people who participated in rice farming were 2.57 times more likely to contract the disease than people who did not farm. Also, people involved in corn farming were 2.5 times more susceptible than those who did not (Marston, Diallo, Horseburgh, Diomande, Saki, Jean-Marie, et al., 1995).

The third environmental factor involving water sources is thought to be related to certain aquatic insects such as the *Naucoris* and *Dyplonychus* species which could be carriers, as well as the *Aplocheilichthys* fish and surrounding vegetation that could live in symbiosis with the disease-causing organism (Eddyani, Ofori-Adjei, Teugels, De Weirdt, Boakye, Meyers, & Portaels, 2004).

The fourth environmental factor is modification of the physical environment. Research suggests that endemic areas which have had a large degree of environmental modification also have a higher prevalence of cases. For example, in Benin, the rate of Buruli ulcer in environmentally modified areas was 180 per 100,000 compared to 20 per 100,000 in areas without (Asiedu et al., 2000). Environmental modification can range from deforestation, dam and road building, to farming and mining. Finally, recent research has suggested that arsenic levels in the soils can have a direct impact on the number of Buruli ulcer cases. Duker, Carranxa, and Hale (2004) found that the areas with arsenic-enriched soils had higher prevalence rates than areas without (Duker et al., 2004).

Land elevation also correlates with Buruli ulcer prevalence. Areas that are low lying have been shown to have a higher incidence of Buruli ulcer while areas of higher elevation have shown a lower incidence of Buruli ulcer prevalence. This occurs because of relationship with low lying areas being catchments for water and other materials, for example arsenic (Duker et al., 2004).

These factors represent the current state of knowledge on variables associated with Buruli ulcer prevalence within specific regions. Due to the lack of definitive variables, further research is ongoing in this field to identify reservoir, transmission, etiology, and possible risk factors. Case control studies have been used to determine risks of an individual, but there is a void in geographical studies that tie all the hypothesized risk factors together in a model for predicting the prevalence in an area. Finally, research has not been conducted to create a geographic representation that can be applied to varying regions to help societies anticipate outbreaks and possible numbers of cases. This is the goal of this study – to develop a geographic model for estimating the prevalence of Buruli ulcer. Data from the national case search conducted by the Center for Disease Control (CDC) in Ghana is used to develop a model of BU prevalence. Such a model can be used to estimate BU prevalence in other endemic areas. This is important because BU occurs in remote rural areas with limited access to health care facilities and underreporting is considered a major problem (WHO, 2006).

Hypotheses

Hypothesis 1: Proximity to slow moving water is a risk factor. Communities that live close to slow moving water will have higher prevalence rates of Buruli ulcer.

Hypothesis 2: Living in low elevation differential areas is a risk factor. Communities that live in lower elevation differentials will have a higher prevalence of Buruli

Hypothesis 3: Soil land cover is negatively associated with Buruli ulcer. Areas with higher degree of soil will have a lower risk of Buruli ulcer compared to other areas.

Hypothesis 4: Human disruptions of the natural physical environment such as deforestations and mining usually coincide with high rates of Buruli ulcer. Thus locations with a high degree of human impact will have a higher prevalence of Buruli ulcer.

Hypothesis 5: Living in rural areas is a risk factor. Communities that live in rural areas will have a higher prevalence of Buruli.

CHAPTER 3

METHODOLOGY

Study Area

The study area for this research is located within the West African country of Ghana in the southwest portion of the country. Ghana (Figure 4) is a country of 22,409,572 people bordering the Gulf of Guinea, between Cote d'Ivoire and Togo encompassing 92, 456 sq miles. The climate of Ghana ranges from a warm area that is mostly dry along the southeast coast; hot and humid in the southwest, to hot and dry in the northern portion of the country. Besides a diverse climate the country also has an elevation ranging from 0 m to 880 m with mostly low plains with a plateau in the south-central area. Land-use of the country is 17.54% arable land, 9.22% permanent crops, and 73.24% other (2005) (CIA Fact book, 2007). An interesting side note is that Lake Volta is the world's largest man-made lake. Demographically, the 22 million plus population average median age is 19.9 years with males being 19.7 and females 20.1 with a per capita GDP estimated in 2006 at $2,600, 20% (1997 est.) unemployment, and 31.4% (1993 est.) of the population below the poverty line (CIA Fact book, 2007).

Administratively Ghana is divided into 10 regions (Ashanti, Brong-Ahafo, Central, Eastern, Greater Accra, Northern, Upper East, Upper West, Volta, and Western) and 110 districts. For this study 42 districts (Figure 5) encompassing 23,516.98 sq. miles located in the southwestern coastline will be used.

Figure 4: Map of Ghana.

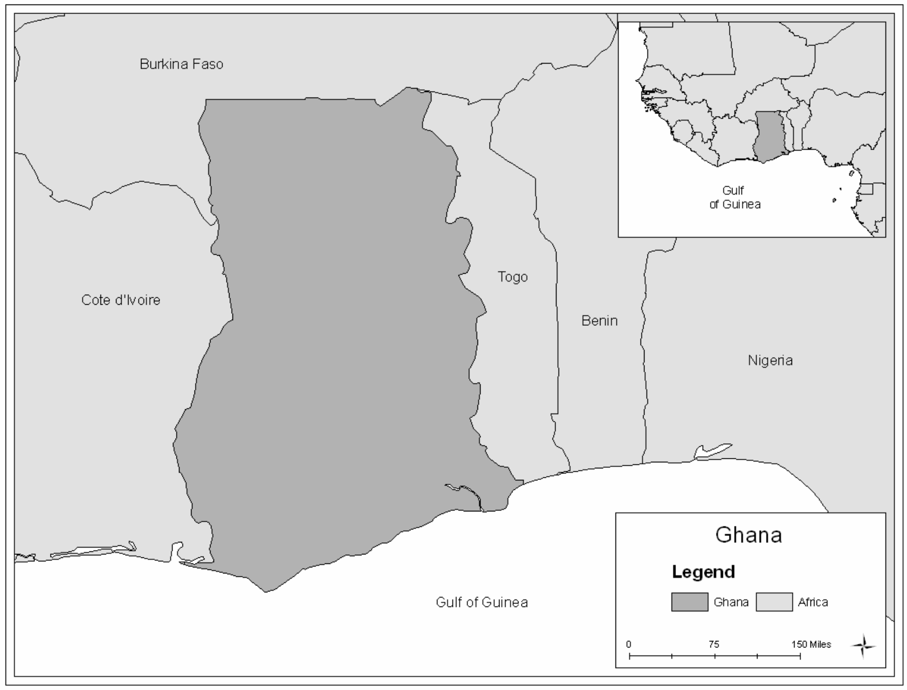
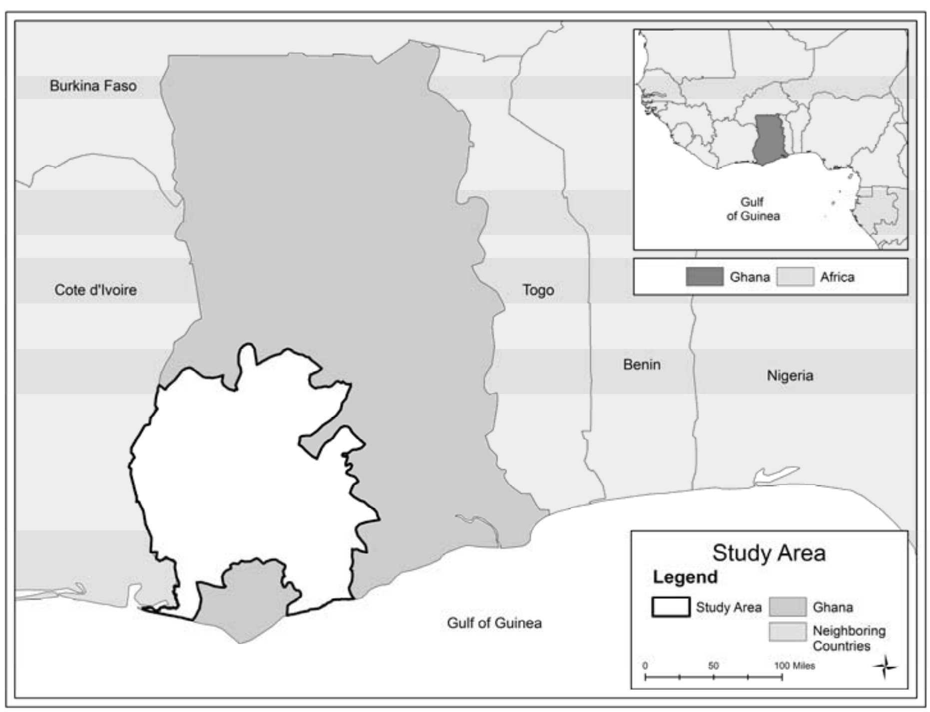


Figure 5: Map of study area.



Data

To create a comprehensive database for this thesis a myriad of data source had to be pulled together that includes rivers, lakes, elevation, demographic, vegetation, and environmental modification to test the hypothesis.

Buruli ulcer case data for this research is derived from the national case search conducted by the Center for Disease Control (CDC) in 1999 (Amofah, Bonsu, Tetteh, Okrah, Asamoa, Kingsley, et al., 2002). Amofah et al. (2002) discusses the method used to collect Buruli ulcer case data in Ghana:

> The case search covered every district and known community in Ghana from June to July 1999 and was done by a team of 20 national facilitators who were trained in the use of the survey equipment and in the clinical presentation of the disease in an endemic focus. Two facilitators were then sent to each region to train teams (three from the regional level and two from each district). Seven teams of two persons each from the subdistrict and communities performed the case search. (2)

The case search identified 5,619 patients with 6,332 clinical lesions that were active and over 10,000 cases active and non-active (non-ulcerative and post-ulcerative) (Amofah et al., 2002). For each case, the data set provides information on residential location (region, district, sub-district, community – actual town or village), location of BU on body, gender, age, and issues of reoccurrence; (Table 1) but for this study, the data was aggregated to the district level and then a prevalence rate was created using the 2000 demographic data from the Ghana national census.

Demographic data was obtained in book format from the Ghana Statistical Service for the 2000 Population and Housing Census. Data was digitized in excel format and then incorporated into the database. These variables include total population, percentage male, percentage female, percentage rural and percentage urban for each district within the study area.

Table 1: National case search data.

Date Interviewed	Upper limb	Specify Scar Location
Case ID	Lower limb	BCG Vaccine
Community	Trunk	Well
Sub-District	Head & Neck	Stream or Rivers
District	Other	Borehole
Region	Specify Location	Pipeborn
Age Categories	Pre-ulcer	Pond
Age	Ulcer	Other
Sex	Scar	Specify Water Source Type
Occupation	Deformity	

Source: *Buruli Ulcer in Ghana: Results of a National Case Search*, 2000.

Miles of rivers and shorelines of lakes were created from 1986 national maps. This was done in ArcMap 8.3 software. First they were geo-referenced to administrative boundaries of Ghana that were obtained from ESRI template data. Once geo-referenced the maps were digitized and combined into a seamless lakes and rivers database. Then the length of shoreline of all lakes were calculated and miles of rivers for each district within the study area. Once the water source file was created the average length of water source per square mile was created for each district to give a more uniform measure to the data.

Human footprint on the environment was obtained through the Columbia Universities Center for International Earth Science Information Network (CIESIN). "The human footprint dataset of the Last of the Wild Project, Version 1, 2002 (LWP-1) is the human influence index (HII) normalized by biome and realm. The HII is a global dataset of 1-kilometer grid cells, created from nine global data layers covering human population pressure (population density in population settlements), human land use and infrastructure (built up areas, nighttime lights, land use/land cover), and human access (coastlines, roads, railroads, navigable rivers)." (WCS, CIESIN, & CU, 2002) To create the human impact variable for this study zonal statistics were used to calculate the mean human impact within each district.

District boundaries, Regional boundaries, and elevation data was bought from the University of Ghana Department of Geography in 2005. Elevation data was in ranges, but for this research the elevation differential was created for each district within the study. Elevation differential measures the difference between the highest and lowest points in each district. This gives a more uniform measure of elevation between each district within the study area.

Vegetation data was created using remote sensing techniques to determine the dominant vegetation type in each spatial unit of the study area. ERDAS software was used to classify the Landsat TM+ Bands 1, 2, 3, 4, 5, & 7 for the four tiles (Table 2) covering the study area. Nine land cover types were classified: water body, forest reserve, light forest, sparse vegetated, soil, urbanized, cloud, cloud shadow, and grass. Classification was carried out by analyzing the different combinations of the Landsat bands, vegetation type maps for Ghana, land use type maps, common knowledge, and creating a normalized difference vegetation index (NDVI). Once classified, they were blended into a mosaic to form one seamless raster file and the percentage of each type of classification was calculated using a spatial analysis tool in Arcmap at the district level.

Accuracy assessment was conducted on 194_055, 194_056, 195_055, and 195_056 to evaluate the accuracy of the classification using thirty randomly selected points for each tile. The accuracy assessment found that the classification of tile 194_055 was 83.33% and kappa statistics of 0.7797 (Table 3). Accuracy assessment for 194_056 was 90% and the kappa statistics of 0.8716 (Table 3). Accuracy assessment of the classification on 195_055 was 83.33% and a overall kappa statistics of 0.7922 (Table 3). Accuracy assessment of the supervised classification for 195_056 was 73.33% and a kappa statistics of 0.6657 (Table 3). Overall accuracy of the four tiles was 82.50% with a kappa statistics of 0.7773 (Table 3) using 120 randomly selected points.

Table 2: Landsat Enhanced Thematic Mapper+.

Scene ID	Satellite	Path	Row	Date of Acquisition	Correction Level
LE7194055000305050	Landsat 7	194	55	February 19, 2003	Systematic
LE7195056000003359	Landsat 7	195	56	February 2, 2000	Systematic
LE7195055000235850	Landsat 7	195	55	December 24, 2002	Systematic
LE7194056000201550	Landsat 7	194	56	January 15, 2002	Systematic

Source: USGS, 2005.

Table 3: Accuracy Assessment

Tile	Accuracy	Kappa Statistics
194_055	83.33%	0.7797
194_056	90%	0.8716
195_055	83.33%	0.7922
195_056	73.33%	0.6657
Total	82.50%	0.7773

Source: Erdas, 2007.

Method

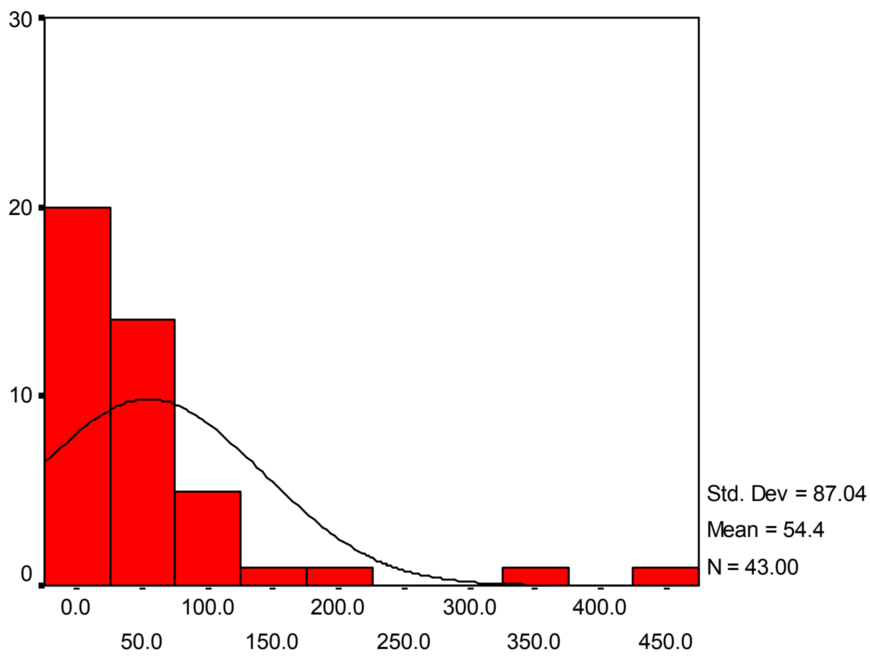
Descriptives

Descriptives of percent rural population, proximity to water source, elevation differential, human footprint, and land cover explored in SPSS statistical software. Age (15 and under, 16 to 50, and 50+), gender, and types of water sources nearby (well, stream or rivers, boreholes, pipeborn, ponds, and other) explored within SPSS to identify the relationships between these values and Buruli ulcer prevalence.

Correlations

A correlation's test was performed on Buruli ulcer prevalence, percent rural population, major water source, elevation differential, human footprint, and land cover to explore their relationships. Spearman's correlation is a non-parametric measure of correlation that measures the difference between two sequences of values. The two sequences are ranked separately and the difference in rank are then calculated at each position to test if there is a relationship. This relationship will range from -1 to 1 (McGrew & Monroe, 2000). Spearman's correlations were chosen because Buruli ulcer prevalence was non-parametric (Figure 6); using the test for normality.

Figure 6: Buruli ulcer prevalence histogram.



Regression

Three methods of regression are used to determine the level of explanation of Buruli ulcer prevalence using the hypothesized factors standard linear regression, spatial lag, and spatial error. Standard linear regression was calculated using SPSS. Spatial lag and spatial error were calculated using GeoDa software with a rook contiguity weight (looks at the neighbors to the north, south, east, and west) that included all lower orders.

Standard linear regression examines the linear relationship between a dependent variable and a set of explanatory variables. This model does not take into account the spatial dependency of neighboring sites, but spatial lag and spatial error do. This is represented in the following equation:

$$y = a + \beta X + \varepsilon$$

y: dependent variable

a: constant

X: independent (explanatory) variables

β: regression coefficients

ε: random error term

Spatial lag looks at the possible diffusion process of events in one place and can predict an increased likelihood of the event occurring in neighboring areas. For example, in this study one district's Buruli ulcer prevalence can be affected by variables in a neighboring district.

> Essentially spatial lag averages the neighboring values of a location (the value of each neighboring location is multiplied by the spatial weight and then the products are summed). It can be used to compare the neighboring values with those of the location itself. Which locations are defined as neighbors in this process is specified through a row-standardized spatial weights matrix in GeoDa. By convention, the location at the center of its neighbors is not included in the definition of neighbors and is therefore set to zero. (Anselin, 2003)

Spatial lag can presented as:

$$y = pWy + X\beta + \varepsilon$$

y: dependent variable

X: independent (explanatory) variables

β: regression coefficients

ε: random error term

ρ: spatial autoregressive coefficient

Wy: spatially lagged dependent variable

Spatial error looks at how the error terms across different spatial units is correlated. “With spatial error in ordinary least squares (OLS) regression, the assumption of uncorrelated error terms is violated. As a result, the estimates are inefficient. Spatial error is indicative of omitted (spatially correlated) covariates that if left unattended would affect inference" (GeoDa, 2007). This is represented in the following equation:

$$y = X\beta + \varepsilon, \text{ where } \varepsilon = \lambda W\varepsilon + \xi$$

y: dependent variable

X: independent (explanatory)

β: regression coefficients

ε: random error term

λ: autoregressive coefficient

Wε: spatial lag for the errors

ξ: normal distribution with mean 0 and variance σ

Assumptions and Potential Errors

Limitations can and do occur when working with medical data, particularly that from the developing world. Access and quality of the data available are problems. One limitation and potential source of error is the matching up of Twi with English names of villages and districts. There are discrepancies between the district names and what is recorded in the national case search. Another is the compromised scale of detail from studying the data at a district level instead of at the village level; the latter is not even possible because of a lack of demographic data at the village level. Finally, there are problems with spelling in the national case search data. The recorded region or district of the patient does not match in some cases. For example, the district recorded for the cases may not match the region in the geographic database. This problem is not unique to this study, but a general problem in geographic research – multiple names – same location, or different locations with similar names. See Maffini, Arno, and Bitterlich in the *Accuracy of Spatial Databases* for a good discussion of this problem (Maffini, Arno, & Bitterlich, 1992).

CHAPTER 4

ANALYSIS

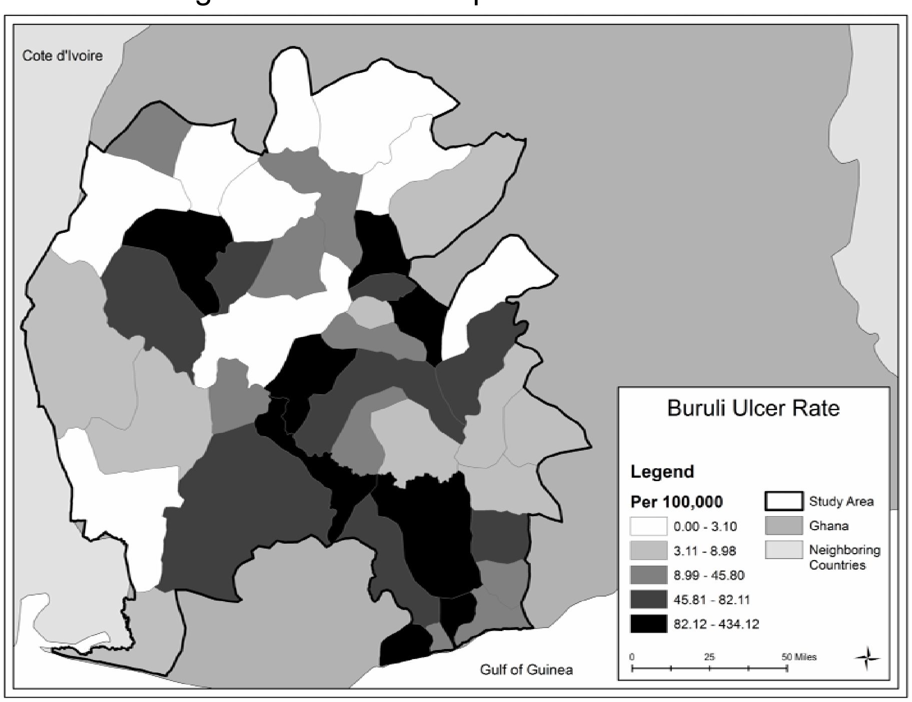
Descriptives

Descriptive statistics of all variances in the study are presented below.

Buruli Ulcer Prevalence

Buruli ulcer prevalence ranges from no cases in six of the districts to 434.12 per 100,000 in the Amansie West district (Figure 7), within the study area the average prevalence is 55.62 per 100,000. This is almost three times the national crude prevalence of 20.7 per 100,000 (Amofah et al., 2002). Amansie West district is twenty one times the national crude rate which could represent better reporting within the district. The highest rates occur in the central and southern portions of the study area. While the lowest rates are seen in the northern and western portions (Figure 7).

Figure 7: Buruli ulcer prevalence.



Age – Gender

Within the study area the average age of Buruli ulcer cases is 33.26 with a standard deviation of 87.72. Males comprised 53.1% of cases and 46.9% were female (Table 3). A cross tabulation of age and gender shows that 34.8% of all cases are fifteen and under, between the age 16 and 50 represented 36.9% of all cases, and fifty plus represented 28.3% of cases. Furthermore, throughout all age categories men outnumber women, compared to the national average which shows females representing 49% of cases and the median age of 25 (Amofah et al., 2002).

Table 4: Sex and Gender

		Sex		
Age		Male	Female	Total
<=15	%	19.6%	15.2%	34.8%
	Cases	394	306	700
15 to 50	%	18.6%	18.3%	36.9%
	Cases	300	269	569
50+	%	14.9%	13.4%	28.3%
	Cases	375	369	744
Total	%	53.1%	46.9%	100.0%
	Cases	1069	944	2013

Source: *Buruli Ulcer in Ghana: Results of a National Case Search*, 2000.

Water Source at Case Level

Since the source of drinking water is a hypothesized risk factor, frequencies of the major source of drinking water were compiled and presented (Table 2). Streams or rivers (54%) and boreholes (52%) were the most popular sources of drinking water. Wells accounting for (24%), pipeborn water was (19%), ponds were used by (9.6%), and other (5%) used others sources of drinking water. Some communities used multiple sources of water, sometimes simultaneously or at different times of the year.

Table 5: Type of water source.

Type of Water Source	Percentage
Well	23.60%
Stream or Rivers	54.20%
Borehole	52.30%
Pipeborn	19.10%
Pond	9.60%
Other	5%

Source: *Buruli Ulcer in Ghana: Results of a National Case Search*, 2000

Percentage Rural

Rural population for the study area was 69.9% of the population with a standard deviation of 18.2%. The lowest percentage rural population is 26% which is the Sunyani district and the highest percentage rural population is 100% rural in the Amansie West district. Geographically, a higher degree of rural populations predominate in the western and central portions. More urbanized populations are in the southern portion along the coast and eastern portions of the study area (Figure 8).

Water Source

Proximity to water sources has been shown in the literature to relate to Buruli ulcer prevalence in endemic regions. Within this study the average length of rivers and lakes per square mile is 0.3017 miles with a standard deviation of 0.077. The lowest amount of water source per square miles is 0.0001 miles in the Kwabre district, while the highest degree of water sources per sq miles is 0.58 in Cape Coast district (Figure 9).

Figure 8: Urban/rural populations.

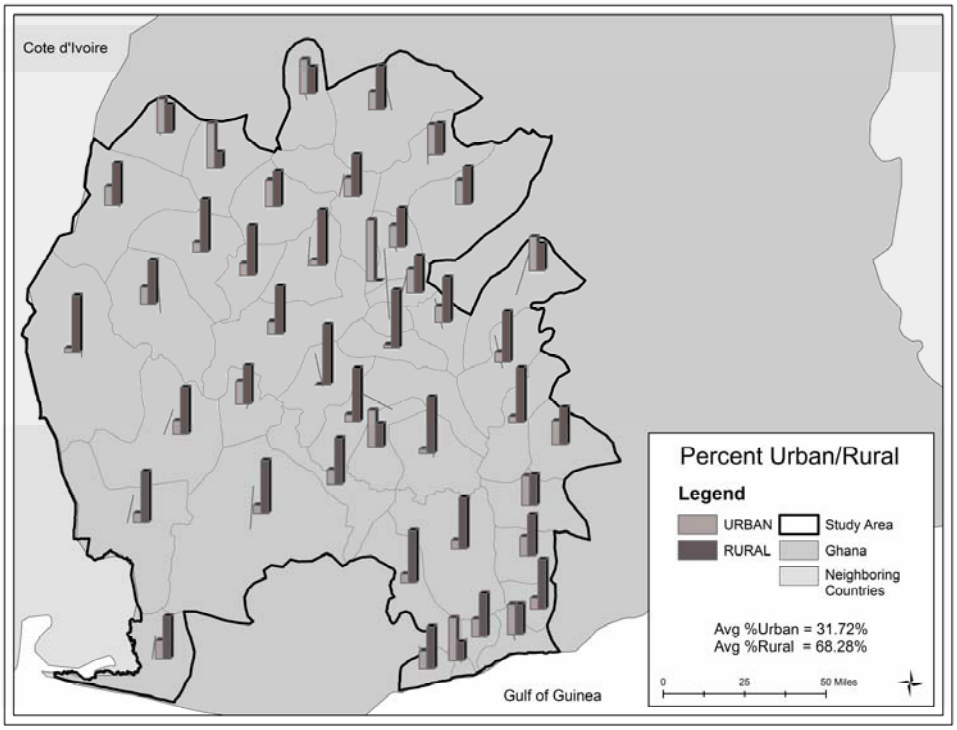
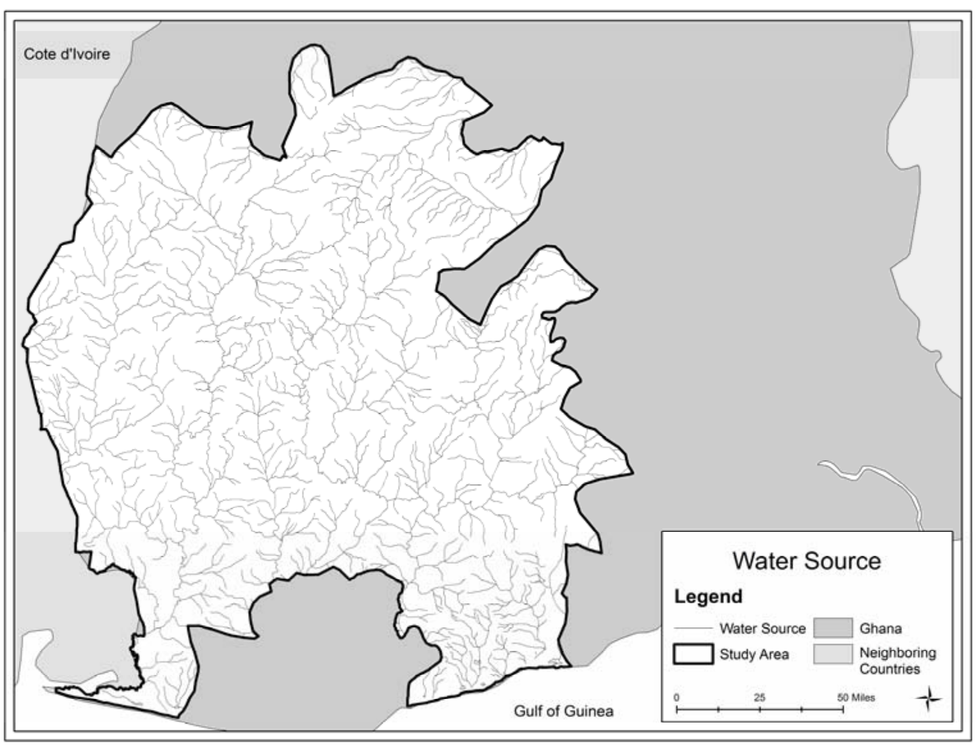


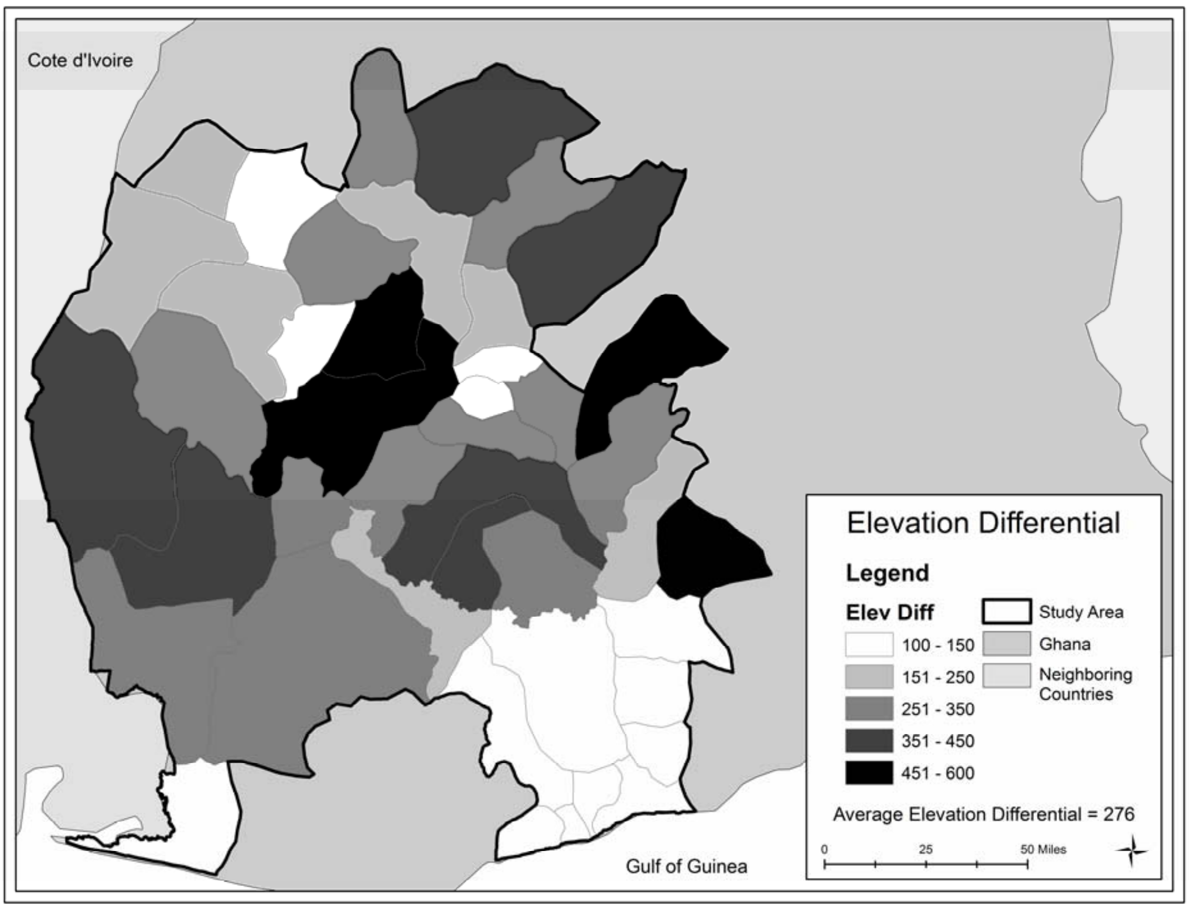
Figure 9: Water source per square mile.



Elevation Differential

The average elevation differential is 280.95 feet with a standard deviation of 130.17. It ranges from 100 ft in Kwaebibirem, Mfantsiman and Cape Coast to the highest elevation differential in Komenda/Edna Eguafo/Ebire district at 600 ft. Geographically, the elevation differential is highest in the central portion and lowest in the southern costal areas (Figure 10).

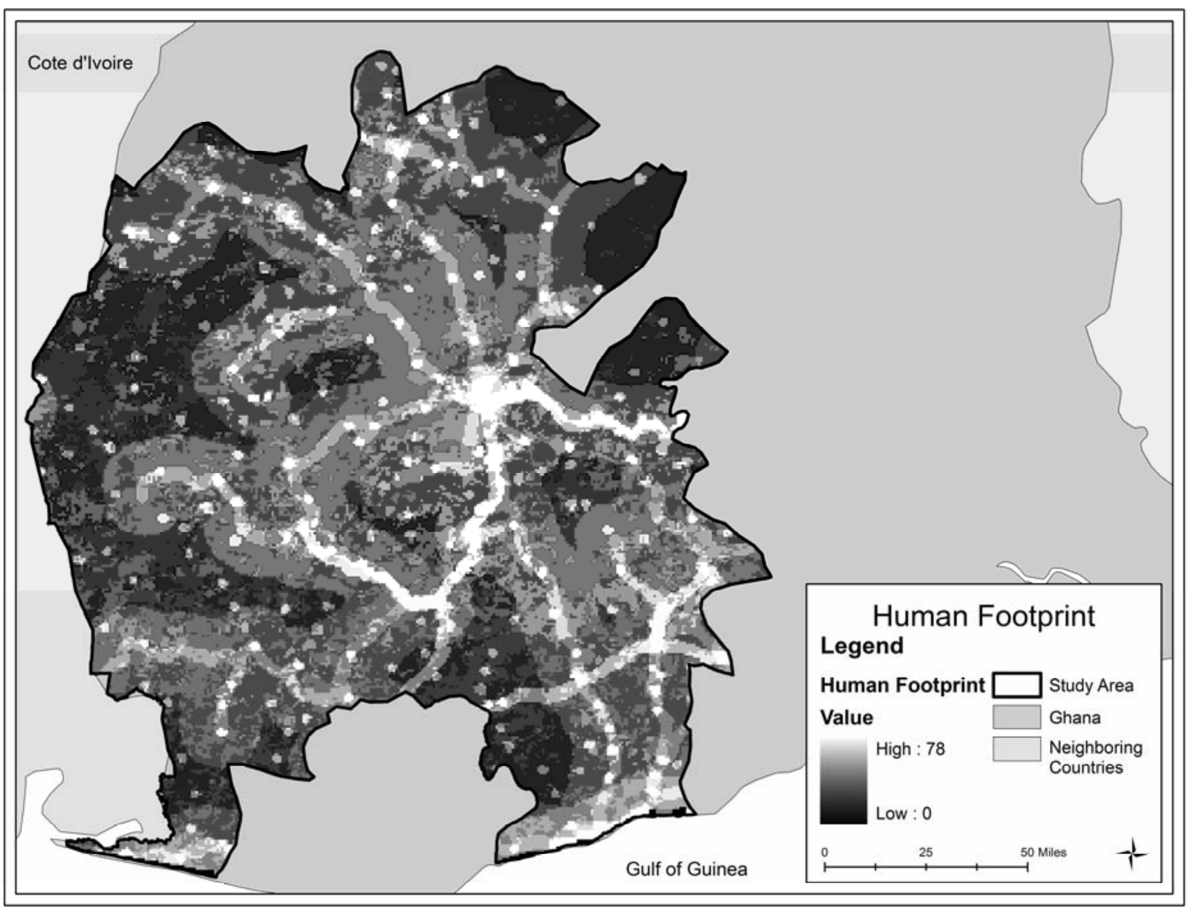
Figure 10: Elevation differential.



Human Footprint

Human impact on the environment is on average 28.13% with a standard deviation of 3.78%. Twifo-Heman/Lower Denkyira district at 20.71% had the lowest degree of human impact and the Cape Coast district at 37.01% has the highest degree of human impact. Geographically, the human impact on the environment is concentrated in the southern, southeast, and central portions of the country. Lowest degree of the human impact is in the western part of the study area along the boarder with Benin (Figure 11).

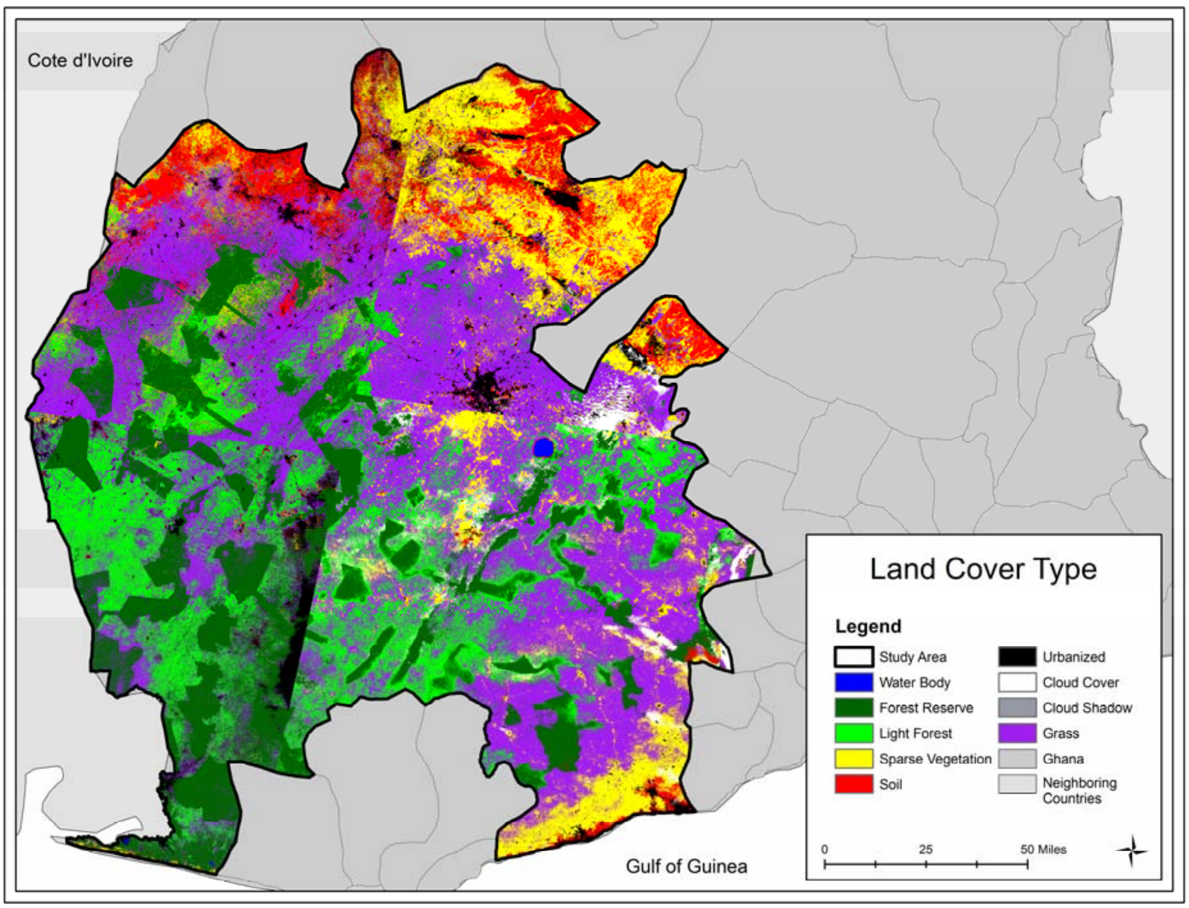
Figure 11: Human footprint.



Soil Land Cover

Soil covers on average 6.7% of the study area with a standard deviation of 10.8%. Birim North has the lowest degree of soil as land cover at 0% and Berekum had the highest percentage of land cover classified soil at 39.16%. The largest degree of land cover classified as soil is in the northern portion of the country with the lowest degree of land cover classified as soil in the southwestern portion of the country (Figure 12).

Figure 12: Land cover.



Correlations

Spearman's correlations were calculated for the five hypothesized factors to test the relationship against Buruli ulcer prevalence within the study area: percent rural, water source, elevation differential, human footprint, and soil land cover.

Table 6: Spearman's correlation.

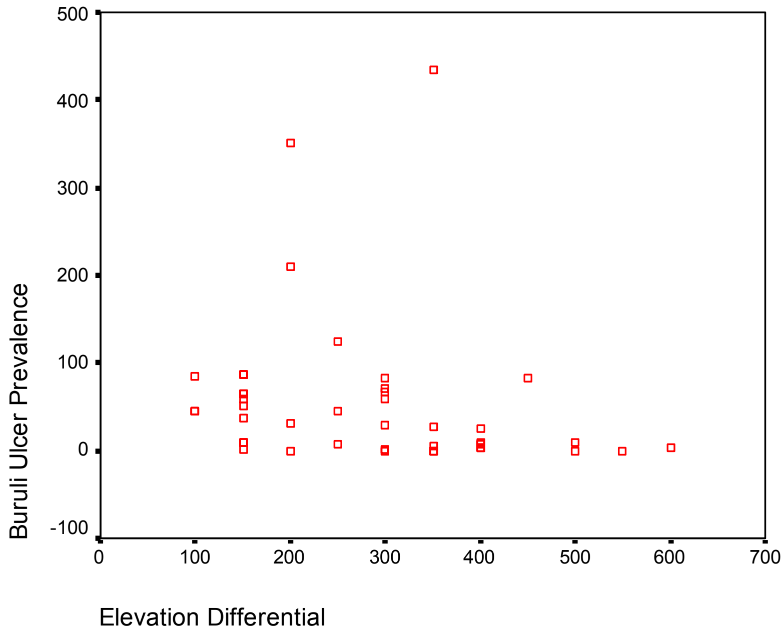
Spearman's			%Rural	Water Source	Elevation Differential	HFP	Soil
Districts	Outliers Not-Removed	Coefficient	0.336*	0.152	-0.429**	0.237	-0.397**
		Sig.	0.03	0.337	0.005	0.131	0.009
		N	42	42	42	42	42
	Outliers Removed	Coefficient	0.286	0.184	-0.477**	0.235	-0.366**
		Sig.	0.073	0.269	0.002	0.144	0.022
		N	40	38	40	40	39
*.Correlation is Significant at the .05 Level (2-tailed). **.Correlation is Significant at the .01 Level (2-tailed).							

Source: Ghana Statistical Services, Columbia University, University of Ghana, USGS, and 1986 Maps, 2006.

Elevation Differential

The Spearman's correlation between elevation differential and the Buruli ulcer (BU) prevalence rate is statistically significant (r = -0.429 = 0.005) (Table 5). The scatter plot (Figure 13) found two outliers existed Amansie West and Upper Denkyira and once removed the relation was (r= -0.477, p= 0.002) (Table 5). Thus areas with high elevation differential have lower Buruli ulcer prevalence rates and districts with lower elevation differential have high Buruli ulcer prevalence rates. This correlation relates to the presence and dominance of water bodies in low lying elevations compared to areas with higher elevations such as mountains. This therefore creates an environment conducive to a higher degree of Buruli ulcer prevalence. Duker et al. (2004) showed that low elevations are more likely to have rivers, marshes and lakes and especially Buruli ulcer. Therefore, populations in areas of lower elevation differential have a greater risk of Buruli ulcer than populations in districts with higher elevation differentials.

Figure 13: Buruli ulcer and elevation differential.

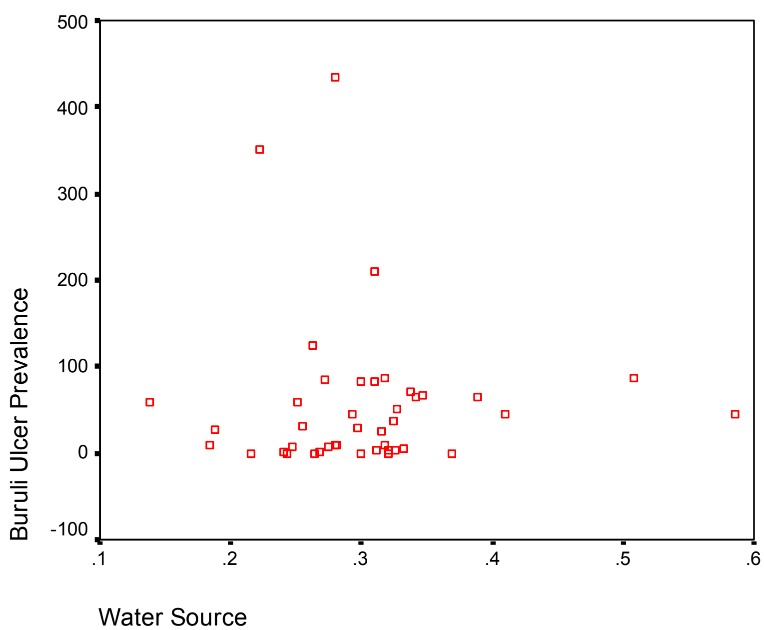


Water Sources

A Spearman's correlation coefficient was performed on the relationship between the average length of rivers and lake shoreline within each district and the Buruli ulcer prevalence rate. A weak correlation that was not statistically significant was found (r = 0.152, p = 0.337) (Table 5). The scatter plot (Figure 14) found four outliers: Amansie West, Upper Denkyira, Cape Coast, and Abura/Asebu/Kwamankese and when removed (r = 0.184, p = 0.269) (Table 5). Proximity to water source is not related to Buruli ulcer prevalence.

This is contrary to what the literature has stated, which is that proximity to water source and Buruli ulcer rates are closely related. Previous research has discussed how areas in close proximity to water bodies such as rivers, lakes, and marshes have a higher prevalence of Buruli ulcer rates than other areas not in close proximity to a water body source. (Reghunathan, Asamoa, & Taylor, 2005; Marston, Diallo, Horseburgh, Diomande, Saki, Jean-Marie, et al., 1995). While this runs contrary to what previous research has shown, it may be simply due to differences in approach for quantifying proximity to a water source at the district level. If more detailed data were available at the district level, or the geographic scale was changed too much a finer scale such as the town level, a more accurate evaluation of this hypothesis could be undertaken. In this study, the absence of a fine measure of proximity to a water body means that only a crude assessment is possible.

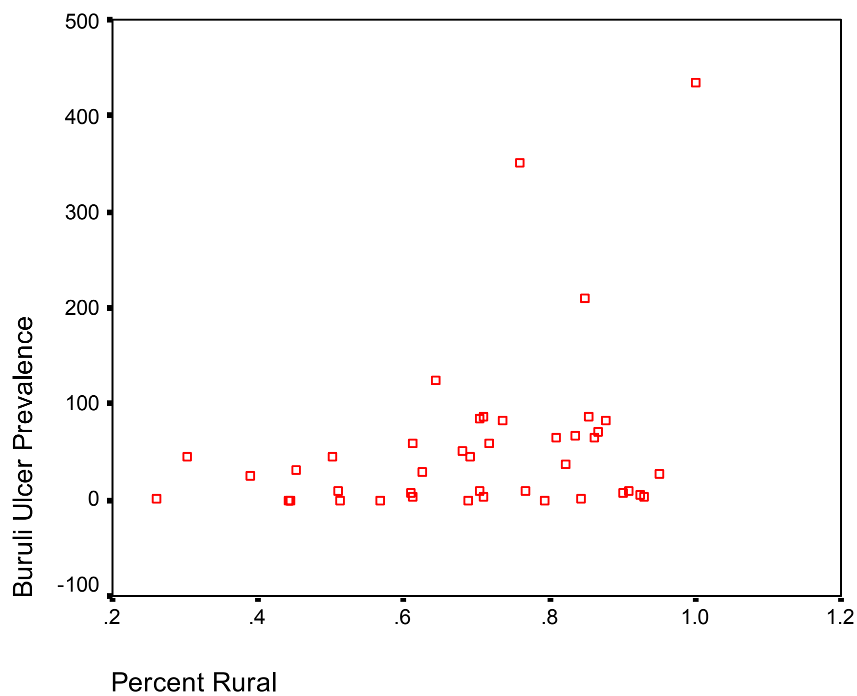
Figure 14: Buruli ulcer prevalence and water sources.



Rural Location and BU

Spearman's correlation coefficient was calculated for the relationship between percentage of rural population within each district and the Buruli ulcer prevalence. A positive correlation that was statistically significant was found (r = 0.336, p = 0.030) (Table 5). Two outliers (Figure 15) were present Amansie West and Upper Denkyira once removed (r = 0.286, p = 0.073) (Table 5). While this is above the significance level of 0.05 it is still noteworthy. Percentage rural is related to Buruli ulcer prevalence within the district which concurs with the available literature. Research by the World Health Organization has discussed how poor rural areas in endemic regions have a higher Buruli ulcer prevalence (WHO, 2006), and these correlations show that within the study area districts with a higher percentage of rural population as defined by the Ghana Statistical Services have a higher Buruli ulcer prevalence rates.

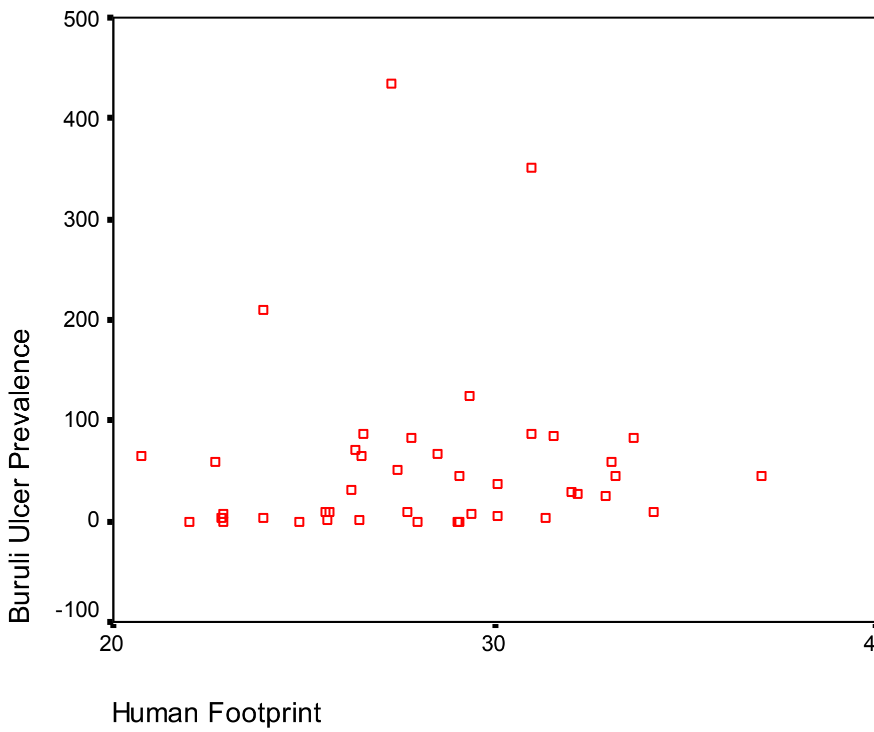
Figure 15: Buruli ulcer prevalence and percentage rural population.



Human Footprint (HFP)

A Spearman's correlation coefficient was calculated for the relationship between the degree of human impact and Buruli ulcer prevalence. A positive correlation that is not statistically significant was found (r = 0.237, p = 0.131) (Table 5). When Amansie West, Upper Denkyira were removed for being outliers (Figure 16) and Spearman's correlation found (r = 0.235, p = 0.144) (Table 5). Thus human footprint is not significantly related to Buruli ulcer prevalence.

Figure 16: Buruli ulcer prevalence and human footprint.



These results contradict the literature. Previous research suggests that the higher the degree of modification to the environment by humans the higher Buruli ulcer prevalence within endemic regions (Asiedu et al., 2000). These results possibly occurred because the human footprint model created by CIESN is a good tool for analyzing the human footprint at global scale but may not work on a more localized scale such as this study. Furthermore, the human footprint model does not include all possible forms of environmental modification by humans.

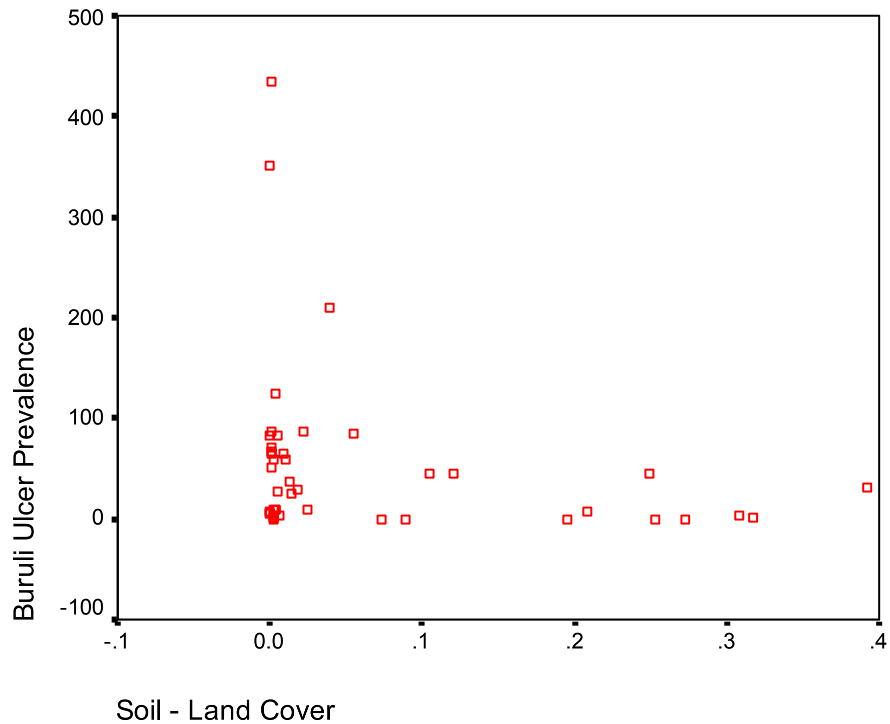
Soil

Spearman's correlation coefficient was run for the relationship between percentage of soil land cover within each district and the Buruli ulcer prevalence. A negative correlation that was statistically significant was found (r = -0.397, p = 0.009) (Table 5). When three outliers Amansie West, Upper Denkyira, and Asutifi (Figure 17) were removed the relationship remained significant, (r = -0.366, p = 0.022) (Table 5) Districts with lower percentage of soil land cover have higher Buruli ulcer rates.

Landsat TM+ remotely sensed data at this scale does not give fine enough detail to accurately differentiate between different grass and sage types. Areas lacking vegetation cover, or more accurately, the lack of vegetation negatively relates to Buruli ulcer prevalence. What this correlation result shows is that districts within the study area with a higher degree of the land cover classified as soil will have lower Buruli ulcer prevalence than areas with less soil as land cover which have higher Buruli ulcer prevalence.

In sum the correlations show significant relationship between Buruli ulcer prevalence and the percent rural, elevation differential, and percent soil land cover. But the human footprint and proximity to water source were not significant.

Figure 17: Buruli ulcer prevalence and percentage soil.



Regression

Classical, spatial lag, and spatial regression models were applied to examine the relationship between percent rural population within each district, elevation differential of each district, and percent land cover that was classified as soil as independent variables and on Buruli ulcer prevalence as a dependent variable.

Classic Regression

A multiple linear regression was calculated to predict Buruli ulcer prevalence based on percent rural population, elevation differential, and percent land cover that was classified as soil which were all significant using Spearman's correlation test. The equation was not significant using classical regression techniques ($F(3,38)=2.497$, *p*>.001 with an R-square of .165. Significance was .074. (Table 6). Buruli Ulcer Prevalence = -4.720 +156.79(%Rural)-.162(Elevation Differential)-49.620(Soil) (Table 7). Buruli ulcer prevalence increased 156.79 for every one percentage point increase in rural population, reduced for -.162 in feet of elevation differential, and reduced by 49.620 in every percentage increase in soil land cover. This model explains 16.2% of Buruli ulcer prevalence within the study area.

Table 7: Multiple linear regression results - ANOVA

ANOVA[b]

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	51953.049	3	17317.683	2.497	.074[a]
	Residual	263589.5	38	6936.566		
	Total	315542.6	41			

a. Predictors: (Constant), Soil - Land Cover, Elevation Differential, Percent Rural

b. Dependent Variable: Buruli Ulcer Prevalence

Source: Ghana Statistical Services, University of Ghana, and USGS, 2006.

Table 8: Multiple linear regression results - coefficients

Coefficients[a]

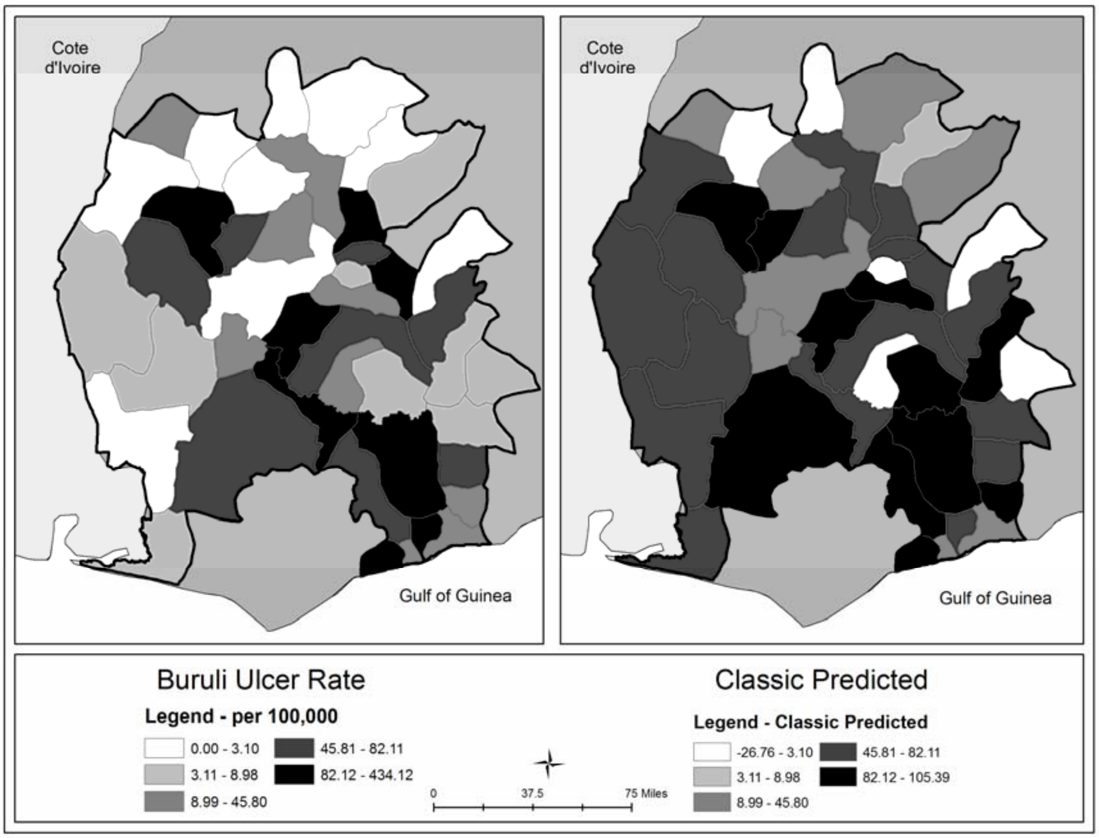
Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	-4.720	75.501		-.063	.950
	Percent Rural	156.279	95.185	.324	1.642	.109
	Elevation Differential	-.162	.102	-.241	-1.594	.119
	Soil - Land Cover	-49.620	157.044	-.061	-.316	.754

a. Dependent Variable: Buruli Ulcer Prevalence

Source: Ghana Statistical Services, University of Ghana, and USGS, 2006.

A geographic representation of this model (Figure: 18) shows the predicted created by the classic regression model. When comparing the actual Buruli ulcer rate to the predicted there is under reporting occurring in the central and southern districts of the study area and over reporting occurring mainly along the western portion of the study area.

Figure 18: Classical regression predicted.



Spatial Lag Regression

A spatial lag regression model was calculated to predict BU rates in the districts based on percent rural, elevation differential, and percent soil land cover.
The equation was not significant using spatial lag regression techniques with an R-square of .197. Buruli Ulcer Prevalence = -27.65074 +166.493(%Rural)-.164(Elevation Differential)-14.913(Soil) (Table 8). This model explains 19.7% of the Buruli ulcer

prevalence within the study area.

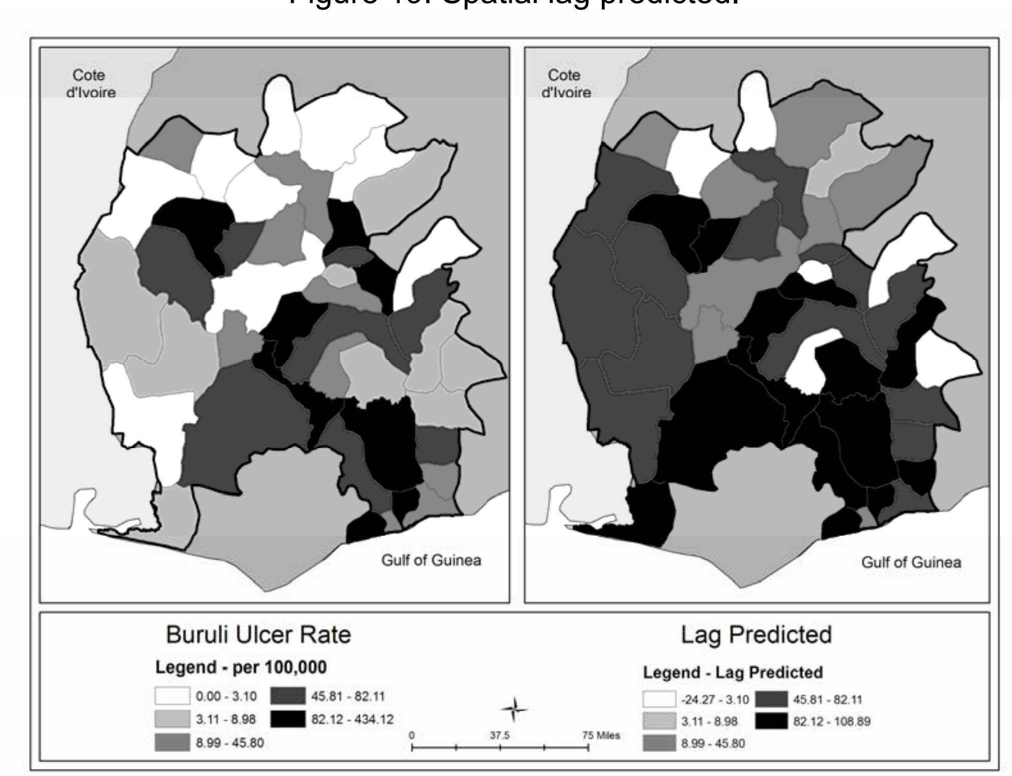
Table 9: Spatial lag regression coefficients.

Variable	Coefficient	Std.Error	z-value	Probability
Buruli Ulcer Prevalence	0.23	0.19	1.22	0.22
Constant	-27.65	72.91	-0.38	0.70
%Rural	166.49	88.82	1.87	0.06
Elevation Differential	-0.16	0.10	-1.73	0.08
%Soil - Land Cover	-14.91	148.40	-0.10	0.92

Source: Ghana Statistical Services, University of Ghana, and USGS, 2006

The geographic representation of the predicted Buruli ulcer rates (Figure 18) show underreporting in the in the southern, central and northern portions of the study area. Furthermore, over reporting of cases is occurring along the western portion of the study area which follows closely to what was shown in the classical regression maps.

Figure 19: Spatial lag predicted.



Spatial Error Regression

Spatial error regression model was calculated to predict Buruli ulcer rates based on percent rural, elevation differential, and percent soil land cover. The model was not significant using spatial error techniques with an R-square of .205. Buruli ulcer Prevalence = -3.88 +159.33(%Rural)-.0.18(Elevation Differential)-31.66(Soil) (Table 9). The spatial error regression model explains 20.5% of Buruli ulcer prevalence within the study area.

Table 10: Spatial error regression coefficients.

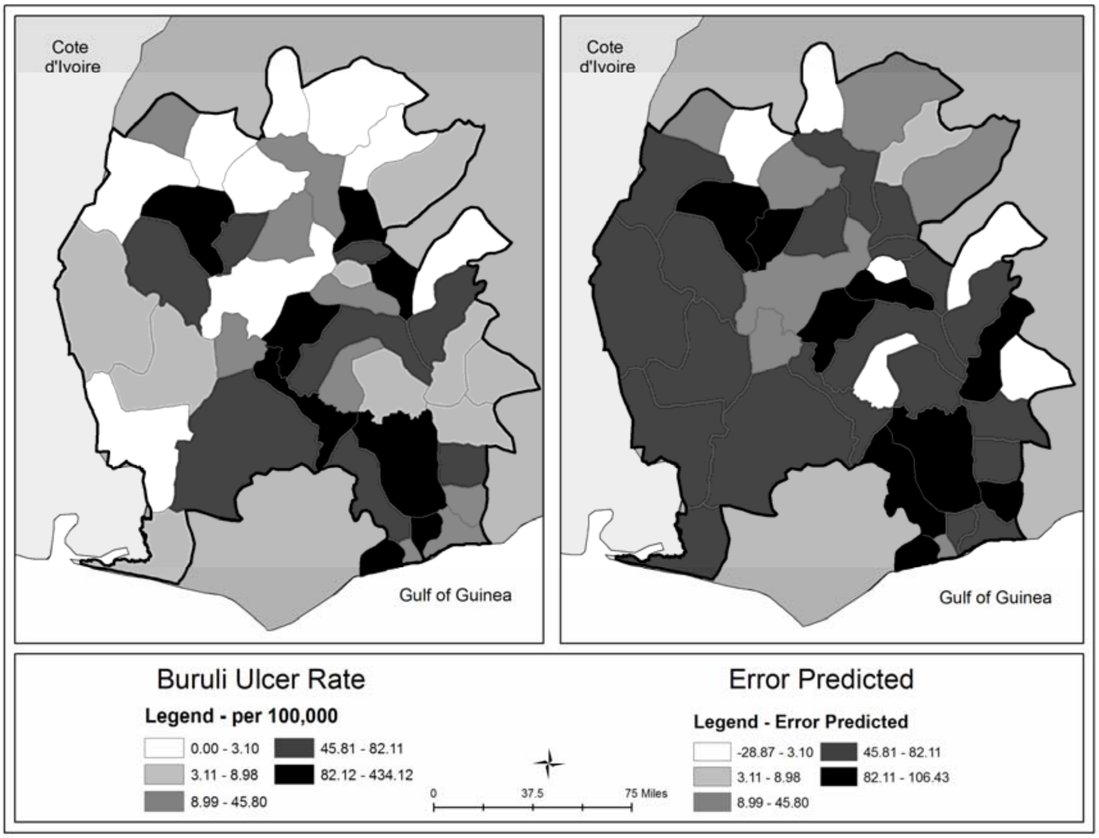
Variable	Coefficient	Std.Error	z-value	Probability
Constant	-3.88	70.37	-0.06	0.96
%Rural	159.33	85.66	1.86	0.06
Elevation Differential	-0.18	0.10	-1.78	0.07
%Soil - Land Cover	-31.66	157.55	-0.20	0.84
Lambda	0.26	0.19	1.36	0.17

Source: Ghana Statistical Services, University of Ghana, and USGS, 2006

Geographic representation of the predicted Buruli ulcer rates (Figure 19) show that underreporting is occurring along the same general locations as the spatial lag model along the southern, central and northern boarders of the study area. Over reporting is occurring along the western part of the study area.

Classical, spatial lag, and spatial error regression models explain 16.5%, 19.7%, and 20.5% respectively of Buruli ulcer prevalence within the study area. While the level of explanation is low, placed in the context of the human ecology mode, these three factors are environmental factors which represent one of the three components of the human ecology model. The human ecology model states that a disease is affected by three components: behavior, environment and genetics. (Meade & Earickson, 2000).

Figure 20: Spatial error predicted.



Conclusion

This analysis shows that while not all suspected factors have been confirmed, several important factors have. The first of these factors is that a percentage of the population within each district that is rural relates to Buruli ulcer prevalence of the district. Secondly, the elevation differential of the district relates to the Buruli ulcer prevalence; districts with lower elevation differential have higher Buruli ulcer prevalence. Finally, percentage of land cover that is classified as soil relates to Buruli ulcer prevalence. Furthermore, these three factors can explain up to 20.5% of Buruli ulcer prevalence within the study area.

CHAPTER 5

DISCUSSION

Hyptheses

Proximity to Water

The first hypothesis was that living in close proximity to water bodies such as lakes was a risk factor for Buruli ulcer. This research found no relationship between proximity to water bodies and Buruli ulcer prevalence. The discrepancy may be due to a difficulty in measuring proximity to water bodies at the district level. The fine details needed to accomplish this were not available at the district level. Consequently, this study only measured the proximity to water bodies using major rivers and lakes, not other suggested measures of water bodies such as marshes, small ponds, and boreholes.

In future research, a different measure of proximity to water bodies maybe necessary. Using some form of distance weighted raster or voronoi model could give a more accurate measure of proximity. The second direction for research would be to increase the level of detail. This would involve finding a way to measure other types of water bodies, such as boreholes, marshes, and ponds. One way of doing this is conducting a detailed survey of the region to find an accurate measure of the interaction with different water sources. Finally, a possible route for future research would be to change the scale of the study to the community level where a finer measure of proximity could be used on the distance to water sources, but this is only possible with more detailed census information. This would allow distance to water bodies to be computed for every community in the study area instead of just for the district as a whole.

While this variable does not have a significant relationship with the disease what it does show is the difficulties of measuring water sources at the district level, and with future research the interaction can be tested.

Elevation Differential

The second hypothesis is that living in low elevation differential areas is a risk factor. Communities with lower elevation differentials were shown to have higher Buruli ulcer prevalence. Areas with low elevation differential represent locations where water catchments and marshes, for example, typically exist and represent a source for BU in relationship to elevation differential. One possible improvement would be to obtain a more detailed measure of elevation using more precise methods, such as digital elevation models.

Land Cover

It was hypothesized that areas with higher degree of specific vegetations types will have a higher risk of Buruli ulcer compared to other areas. The results confirmed a strong negative correlation between the amounts of soil observed within each district and Buruli ulcer rates. The areas with higher soil land cover had lower BU rates, and lower soil land cover had higher BU rates.

Percentage of soil land cover was used to test the hypothesis, because the level of detail of the nine classifications could not differentiate between major land cover types. Greater detail is needed, because past research has hypothesized that the BU reservoir probably lives in symbiosis with certain vegetation types like *Hyperrhenia*, *Imperata cylindrical*, and *Panicum maxium* that grow in endemic regions (Barker, Clancey, & and Rao 1972).

Future research would need to focus on a more detailed vegetation classification to permit scrutiny of the interaction between specific vegetation types Buruli ulcer. This would require more detailed remote sensing data that could differentiate between different grasses and sages. Ground truthing in the field would also be required to check the accuracy of the classifications, and would improve the ability and accuracy of the model. Expanding the study area to include the entire country would also give a greater diversity of vegetation types and the influence on the disease. Finally, the much larger problem really is the inability of coarse remote sensing data to be used in modeling Buruli ulcer which requires much finer data, such as hyperspectral data that has 288 spectral bands in 400 nm ~ 1000 nm.

Human Footprint

The fourth hypothesis focused on human disruptions of the natural physical environment. Since environmental disturbances such as deforestation and mining usually coincide with high rates of Buruli ulcer, locations with a high degree of human impact were expected to have a higher prevalence of Buruli ulcer. In this study however no correlation was found between Buruli ulcer and human footprint, which contradicts previous research.

This could be due to several reasons. First, the human footprint index (HFI) created by Columbia University does not give a detailed enough analysis of human impact on the environment. HFI looks at utilities, nighttime lights, land cover, transportation, settlements, and built up areas. But the dataset does not include some of the hypothesized factors of environmental modification that could influence Buruli ulcer rates. For example, the variable does not include deforestation which has been shown to increase BU rates. Nor does it include mining, damns, and farming. The inability of the variable to include a more detailed measure of the degree of environmental modification possibly limits the full explanatory potential.

Solutions to this problem would be to create a raster that measures all the environmental modifications that have been hypothesized. But, the difficulty in doing this is the limited availability and limited accuracy of data needed to create a more specific model to calculate the degree of environmental modification. To complicate matters, more specific and fine data would also decrease the generalized ability of the resulting model. To be useful, a model for Buruli ulcer prevalence should use common variables and have an equation that is as simple as possible so that others can use it without too much data manipulation.

Rural Population

The fifth hypothesis is that living in rural areas is a risk factor for Buruli ulcer. There was a significant focus on communities in rural areas having a higher prevalence of BU. This follows current research that rural populations are at greater risk for the disease than urban populations. This is an important factor, because many health services in the developing world are usually located in the urban areas while in rural areas access to health services is limited, at best, or simply non-existent. When the only form of treatment is surgical it is imperative that health resources are focused where it is most needed which are rural areas in endemic regions. Within this study rural populations are at an increased risk and the need for more health services is evident.

Regression

Using simple linear, spatial lag and spatial regression modeling techniques to create a prevalence model for this disease found that 16.5%, 19.8%, and 20.5% of the spatial prevalence respectively were explained. Spatial error model explained the largest percentage at 20.5%. The model is a good learning tool on assessing if underreporting is occurring and what directions to go in the future to fine tune the model. Underreporting of diseases such as Buruli ulcer and HIV/AIDS has been seen as a major problem within the developing world and because of this the impact of the hypothesized factors could be affected.   With a more detailed model an accurate representation of the Buruli ulcer epidemic can be studied.

Problems

Data from the developing world can be problematic. The quality and availability of the data can vary among the datasets. For example, within this study detailed hydrology data was not readily available and had to be hand digitized from 1986 maps; infrastructure data, and detailed demographic data was not available.

Future Research

The first avenue for future research would be detailed census data to look at the relationship between age, sex, and income breakdowns. The importance of this is revealed in literature where it has been shown that different age groups are affected at different rates. For example, children under the age of 15 comprise up to 70% of all cases according to the World Health Organization (WHO, 2006). This would allow further testing within the study area. Gender has also been shown to vary among Buruli ulcer cases. For example, in West Africa previous research states men to be at greater risk than women. The third important benefit of detailed demographic information is to examine the relationship of income to Buruli ulcer rates. While all people have equal risk of getting Buruli ulcer, it would be interesting to see if people with a lower income level had higher Buruli ulcer prevalence; research by the World Health Organization states that the poor are affected at a greater percentage than the wealthy. Furthermore, detailed demographic information will allow a greater degree of analysis to define the population at risk for Buruli ulcer.

The scale of the study needs to be changed to the town/village level instead of aggregated to districts. Detailed demographic data at the village level, changing the scale of the study to towns, and expanding the study area to the entire country could possibly give a better explanation of the disease and its relationship to the hypothesized factors. This would also provide a better measure of proximity to water sources than the current scale of district level allows.

Examining the influence of arsenic levels in the soil is also important. Duker, Carranza, and Hale (2006) showed that areas with higher arsenic levels have higher

Buruli ulcer prevalence's (Duker, 2004). With arsenic data the study by Duker could be replicated and tested again in a new study area. Also, examining relationship of climate and rainfall to Buruli ulcer rates would be an interesting avenue to study. Past research has suggested that climate and temperature could play a role in intensity of the disease across the spatial landscape.

A final avenue for future research would be to conduct spatial cluster analysis. This would look at the difference of the hypothesized factors between high prevalence district clusters compared to districts with low Buruli ulcer rates.

Conclusion

Buruli ulcer prevalence varies geographically in endemic regions. This research has attempted to test the factors that affect Buruli ulcer prevalence spatially and to explore a model that will predict Buruli ulcer prevalence. With previous research suggesting that the disease rates could be influenced by rural location, proximity to water source, elevation, degree of human impact, and land cover. This research tested the five hypothesized factors and used simple linear, spatial lag, and spatial error regression to create a model.

Research found that Buruli ulcer prevalence within each district in the study was influenced by how rural the population is, the elevation differential, and percentage of land cover that is classified as soil. Districts with a higher degree of rural population had higher Buruli ulcer prevalence. Districts with lower elevation differential had higher Buruli ulcer prevalence. Districts with lower percentage soil as land cover had higher

Buruli ulcer prevalence. Buruli ulcer is mainly seen in the southern portion of the study area: the northern part seems to have lower Buruli ulcer prevalence.

Three regression models found that linear regression explained 16.5%, spatial lag explained 19.8%, and spatial error explained 20.5% of Buruli ulcer prevalence within the study area. Spatial error explained the largest percentage of Buruli ulcer rates; therefore, this is the best of the three models for estimating Buruli ulcer prevalence in the study area.

Additional research with finer data should target a more powerful model for estimating Buruli ulcer prevalence and allow more effective deployment of intervention resources. While this study has not been able to accomplish that, it has demonstrated what needs to be done. The poor victims of this incurable disease need all the help they can get. Unfortunately, Buruli ulcer does not affect enough people in the United States to make it a priority for funding and research. How long will the Buruli ulcer victims have to wait?

APPENDIX

SUPPLEMENTAL TABLES AND FIGURES

Table 11: Sex descriptive.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Male	1074	52.9	53.1	53.1
	Female	947	46.6	46.9	100.0
	Total	2021	99.5	100.0	
Missing	System	10	.5		
Total		2031	100.0		

Table 12: Well – water source.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	753	37.1	61.1	61.1
	Yes	479	23.6	38.9	100.0
	Total	1232	60.7	100.0	
Missing	System	799	39.3		
Total		2031	100.0		

Table 13: Stream or river – water source.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	429	21.1	28.0	28.0
	Yes	1101	54.2	72.0	100.0
	Total	1530	75.3	100.0	
Missing	System	501	24.7		
Total		2031	100.0		

Table 14: Borehole – water source.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	529	26.0	33.2	33.2
	Yes	1062	52.3	66.8	100.0
	Total	1591	78.3	100.0	
Missing	System	440	21.7		
Total		2031	100.0		

Table 15: Pipeborn – water source.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	992	48.8	71.9	71.9
	Yes	387	19.1	28.1	100.0
	Total	1379	67.9	100.0	
Missing	System	652	32.1		
Total		2031	100.0		

Table 16: Pond – water source.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	988	48.6	83.5	83.5
	Yes	195	9.6	16.5	100.0
	Total	1183	58.2	100.0	
Missing	System	848	41.8		
Total		2031	100.0		

Table 17: Other – water source.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	508	25.0	83.4	83.4
	Yes	101	5.0	16.6	100.0
	Total	609	30.0	100.0	
Missing	System	1422	70.0		
Total		2031	100.0		

Table 18: Case data descriptive.

Statistics

		Region	Age	Sex	Well	Stream or Rivers	Borehole	Pipeborn	Pond	Other	Specify	Occupation	Upperlimb	Lowerlimb	Trunk	Head & Neck	Other	Age Recode
N	Valid	2031	2019	2021	1232	1530	1591	1379	1183	609	2031	2031	1251	1845	1143	993	630	2019
	Missing	0	12	10	799	501	440	652	848	1422	0	0	780	186	888	1038	1401	12
Mean			33.26	1.47	.39	.72	.67	.28	.16	.17			.26	.84	.07	.08	.05	2.02
Median			27.00	1.00	.00	1.00	1.00	.00	.00	.00			.00	1.00	.00	.00	.00	2.00
Mode			12	1	0	1	1	0	0	0			0	1	0	0	0	3
Sum			67145	2968	479	1101	1062	387	195	101			331	1555	79	76	34	4086

Table 19: Model variable statistics.

	N	Minimum	Maximum	Mean	Std. Deviation
Buruli Ulcer Prevalence per 100,000	42	.00	434.12	55.6602	87.72754
%Male	42	.46	.55	.4983	.01724
%Rural	42	.26	1.00	.6990	.18253
Human Footprint	42	20.71	37.01	28.1338	3.78568
Elevation Differential	42	100	600	280.95	130.175
Water Source	42	.14	.58	.3017	.07724
Soil - Land Cover	42	.0000	.3916	.067483	.1087159
Valid N (listwise)	42				

Table 20: Model correlations.

			Buruli Ulcer Prevalence	Percent Rural	Human Footprint	Elevation Differential	Water Source	Soil - Land Cover
Spearman's rho	Buruli Ulcer Prevalence	Correlation Coefficient	1.000	.336*	.237	-.429**	.152	-.397**
		Sig. (2-tailed)	.	.030	.131	.005	.337	.009
		N	42	42	42	42	42	42
	Percent Rural	Correlation Coefficient	.336*	1.000	-.173	.203	.150	-.718**
		Sig. (2-tailed)	.030	.	.275	.197	.344	.000
		N	42	42	42	42	42	42
	Human Footprint	Correlation Coefficient	.237	-.173	1.000	-.240	-.037	-.059
		Sig. (2-tailed)	.131	.275	.	.126	.814	.709
		N	42	42	42	42	42	42
	Elevation Differential	Correlation Coefficient	-.429**	.203	-.240	1.000	-.045	-.134
		Sig. (2-tailed)	.005	.197	.126	.	.775	.396
		N	42	42	42	42	42	42
	Water Source	Correlation Coefficient	.152	.150	-.037	-.045	1.000	-.146
		Sig. (2-tailed)	.337	.344	.814	.775	.	.358
		N	42	42	42	42	42	42
	Soil - Land Cover	Correlation Coefficient	-.397**	-.718**	-.059	-.134	-.146	1.000
		Sig. (2-tailed)	.009	.000	.709	.396	.358	.
		N	42	42	42	42	42	42

*. Correlation is significant at the .05 level (2-tailed).

**. Correlation is significant at the .01 level (2-tailed).

Table 21: Buruli ulcer prevalence, elevation differential correlation - outliers removed.

			Buruli Ulcer Prevalence	Elevation Differential
Spearman's rho	Buruli Ulcer Prevalence	Correlation Coefficient	1.000	-.477**
		Sig. (2-tailed)	.	.002
		N	40	40
	Elevation Differential	Correlation Coefficient	-.477**	1.000
		Sig. (2-tailed)	.002	.
		N	40	40

**. Correlation is significant at the .01 level (2-tailed).

Figure 21: Buruli ulcer prevalence, elevation differential scatter plot – outliers removed.

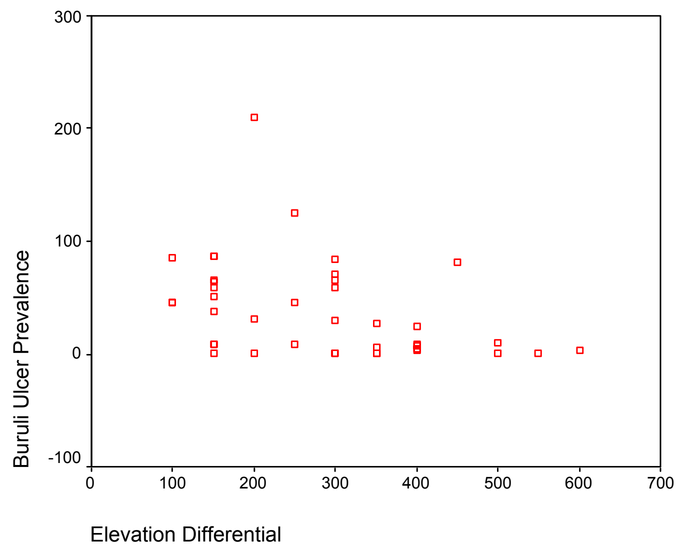


Table 22: Buruli ulcer prevalence, water source correlation - outliers removed.

			Buruli Ulcer Prevalence	Water Source
Spearman's rho	Buruli Ulcer Prevalence	Correlation Coefficient	1.000	.184
		Sig. (2-tailed)	.	.269
		N	38	38
	Water Source	Correlation Coefficient	.184	1.000
		Sig. (2-tailed)	.269	.
		N	38	38

Figure 22: Buruli ulcer prevalence, water source scatter plot – outliers removed.

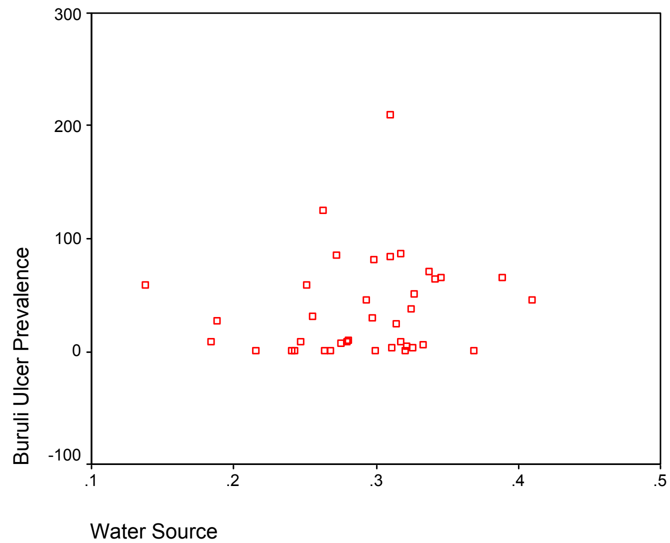


Table 23: Buruli ulcer prevalence, percentage rural correlation - outliers removed.

			Buruli Ulcer Prevalence	Percent Rural
Spearman's rho	Buruli Ulcer Prevalence	Correlation Coefficient	1.000	.286
		Sig. (2-tailed)	.	.073
		N	40	40
	Percent Rural	Correlation Coefficient	.286	1.000
		Sig. (2-tailed)	.073	.
		N	40	40

Figure 23: Buruli ulcer prevalence, percent rural scatter plot – outliers removed.

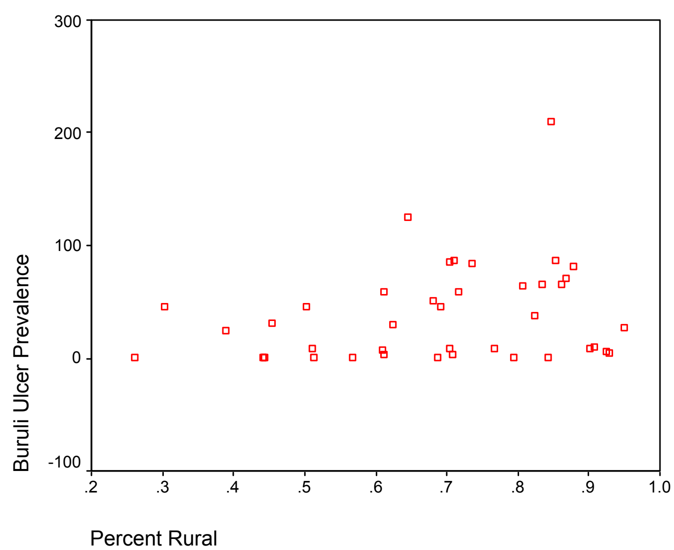


Table 24: Buruli ulcer prevalence, human footprint correlation - outliers removed.

			Buruli Ulcer Prevalence	Human Footprint
Spearman's rho	Buruli Ulcer Prevalence	Correlation Coefficient	1.000	.235
		Sig. (2-tailed)	.	.144
		N	40	40
	Human Footprint	Correlation Coefficient	.235	1.000
		Sig. (2-tailed)	.144	.
		N	40	40

Figure 24: Buruli ulcer prevalence, human footprint scatter plot – outliers removed.

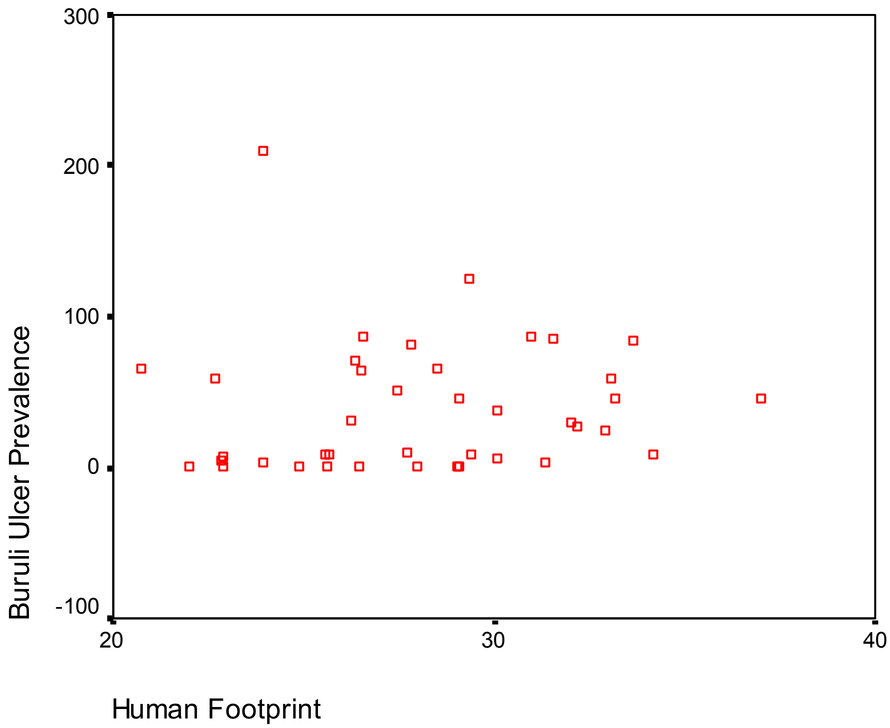


Table 25: Buruli ulcer prevalence, soil land cover correlation - outliers removed.

			Buruli Ulcer Prevalence	Soil - Land Cover
Spearman's rho	Buruli Ulcer Prevalence	Correlation Coefficient	1.000	-.366*
		Sig. (2-tailed)	.	.022
		N	39	39
	Soil - Land Cover	Correlation Coefficient	-.366*	1.000
		Sig. (2-tailed)	.022	.
		N	39	39

*. Correlation is significant at the .05 level (2-tailed).

Figure 25: Buruli ulcer prevalence, soil land cover scatter plot – outliers removed.

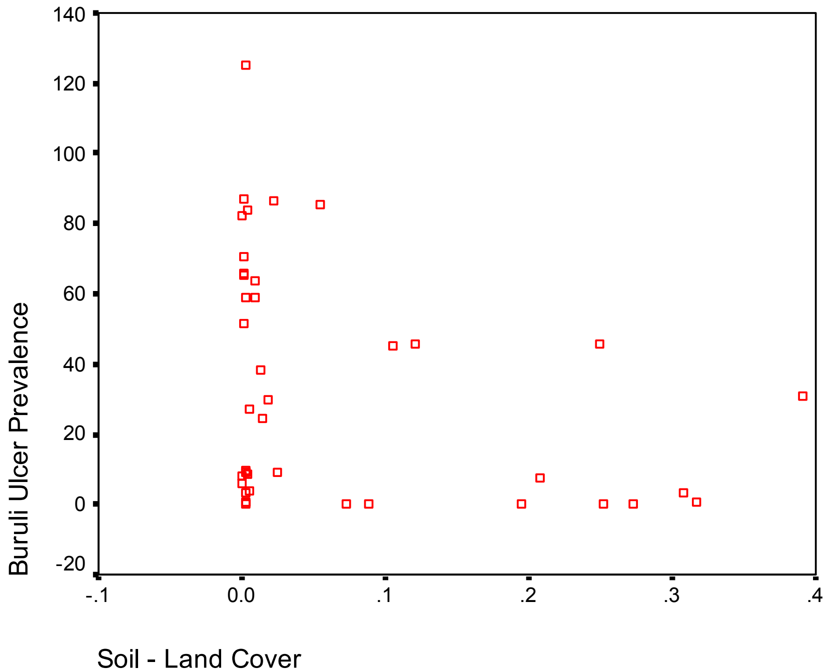


Table 26: Standard linear regression.

Variables Entered/Removed[b]

Model	Variables Entered	Variables Removed	Method
1	Soil - Land Cover, Elevation Differential, Percent Rural[a]	.	Enter

a. All requested variables entered.

b. Dependent Variable: Buruli Ulcer Prevalence

Model Summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.406[a]	.165	.099	**********

a. Predictors: (Constant), Soil - Land Cover, Elevation Differential, Percent Rural

ANOVA[b]

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	51953.049	3	17317.683	2.497	.074[a]
	Residual	263589.5	38	6936.566		
	Total	315542.6	41			

a. Predictors: (Constant), Soil - Land Cover, Elevation Differential, Percent Rural

b. Dependent Variable: Buruli Ulcer Prevalence

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	-4.720	75.501		-.063	.950
	Percent Rural	156.279	95.185	.324	1.642	.109
	Elevation Differential	-.162	.102	-.241	-1.594	.119
	Soil - Land Cover	-49.620	157.044	-.061	-.316	.754

a. Dependent Variable: Buruli Ulcer Prevalence

Table 27: Spatial lag regression results.

REGRESSION SL rook 41507

SUMMARY OF OUTPUT: SPATIAL LAG MODEL - MAXIMUM LIKELIHOOD ESTIMATION

Data set : StudyArea42

Spatial Weight : rook.GAL

Dependent Variable : BU_T_100_0 Number of Observations: 42

Mean dependent var : 55.6602 Number of Variables : 5

S.D. dependent var : 86.6769 Degrees of Freedom : 37

Lag coeff. (Rho) : 0.233077

R-squared : 0.197507 Log likelihood : -242.661

Sq. Correlation : - Akaike info criterion : 495.321

Sigma-square : 6029.04 Schwarz criterion : 504.009

S.E of regression : 77.6469

Variable	Coefficient	Std.Error	z-value	Probability
W_BU_T_100_0	0.2330774	0.1917346	1.215625	0.2241280
CONSTANT	-27.65074	72.91451	-0.3792213	0.7045236
RURAL	166.493	88.81894	1.874521	0.0608585
ELEV_DIFF	-0.1643024	0.09509119	-1.72784	0.0840168

SOIL_COMB	-14.9131	148.403	-0.1004906	0.9199547

REGRESSION DIAGNOSTICS

DIAGNOSTICS FOR HETEROSKEDASTICITY

RANDOM COEFFICIENTS

TEST	DF	VALUE	PROB
Breusch-Pagan test	3	27.90065	0.0000038

DIAGNOSTICS FOR SPATIAL DEPENDENCE

SPATIAL LAG DEPENDENCE FOR WEIGHT MATRIX : rook.GAL

TEST	DF	VALUE	PROB
Likelihood Ratio Test	1	1.114493	0.2911073

COEFFICIENTS VARIANCE MATRIX

CONSTANT	RURAL	ELEV_DIFF	SOIL_COMB	W_BU_T_100_0
5316.526110	-5755.559594	-1.494610	-7456.496127	-3.809548
-5755.559594	7888.804285	-1.500293	8576.387244	1.407275
-1.494610	-1.500293	0.009042	-1.026881	0.001215
-7456.496127	8576.387244	-1.026881	22023.448724	4.432262
-3.809548	1.407275	0.001215	4.432262	0.036762

OBS	BU_T_100_0	PREDICTED	RESIDUAL	PRED ERROR
1	0	-7.09754	10.00812	7.09754
2	3.1	23.80434	-20.67464	-20.70434
3	31.1	15.80696	22.46410	15.29304
4	0	3.20899	-6.25492	-3.20899
5	0.56	-2.04640	0.96792	2.60640
6	7.68	10.68286	-11.98127	-3.00286
7	0	64.14007	-67.23430	-64.14007
8	45.43	49.70089	-3.19905	-4.27089
9	0	30.22107	-32.21137	-30.22107
10	209.5	91.01222	124.27826	118.48778
11	125.11	44.85869	82.10521	80.25131
12	9.73	53.50350	-38.31469	-43.77350
13	0	-24.27143	21.99774	24.27143
14	63.93	94.28362	-31.26591	-30.35362
15	59.19	57.30641	5.92774	1.88359
16	4.08	75.97307	-61.30686	-71.89307
17	0	28.83672	-36.18634	-28.83672
18	58.91	59.36063	-6.43680	-0.45063
19	83.75	58.11504	26.62338	25.63496
20	66.07	72.19480	-5.29186	-6.12480
21	27.39	87.12956	-80.50164	-59.73956
22	434.12	95.44571	329.96319	338.67429

23	8.1	93.14065	-80.78533	-85.04065
24	8.73	49.10341	-32.42512	-40.37341
25	82.11	61.27024	8.02889	20.83976
26	30.02	43.49256	-37.91314	-13.47256
27	24.74	-10.98523	19.29929	35.72523
28	3.35	-8.15124	26.07378	11.50124
29	350.41	82.32953	257.96555	268.08047
30	6.19	83.68778	-73.32205	-77.49778
31	70.4	83.64292	-16.08220	-13.24292
32	0.84	79.88723	-67.40570	-79.04723
33	8.92	48.92395	-30.59655	-40.00395
34	87.04	108.13848	-21.18482	-21.09848
35	65.25	108.89452	-56.15617	-43.64452
36	51.46	81.13282	-19.85953	-29.67282
37	38.06	103.26709	-60.28850	-65.20709
38	45.8	58.33710	-6.09957	-12.53710
39	8.98	83.25884	-63.52347	-74.27884
40	86.58	83.13362	6.78754	3.44638
41	45.72	25.77974	23.21622	19.94026
42	85.38	87.34758	0.79488	-1.96758

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Table 28: Spatial error regression results.

REGRESSION se rook 41507

SUMMARY OF OUTPUT: SPATIAL ERROR MODEL - MAXIMUM LIKELIHOOD ESTIMATION

Data set : StudyArea42

Spatial Weight : rook.GAL

Dependent Variable : BU_T_100_0 Number of Observations: 42

Mean dependent var : 55.660238 Number of Variables : 4

S.D. dependent var : 86.676876 Degree of Freedom : 38

Lag coeff. (Lambda) : 0.264888

R-squared : 0.205326 R-squared (BUSE) : -

Sq. Correlation : - Log likelihood : -242.538483

Sigma-square : 5970.291135 Akaike info criterion : 493.077

S.E of regression : 77.2677 Schwarz criterion : 500.027644

Variable	Coefficient	Std.Error	z-value	Probability
CONSTANT	-3.880632	70.3664	-0.05514893	0.9560197
RURAL	159.3322	85.66073	1.860038	0.0628801
ELEV_DIFF	-0.1778155	0.09980497	-1.78163	0.0748095

SOIL_COMB	-31.66448	157.5545	-0.2009748	0.8407184
LAMBDA	0.2648882	0.1941877	1.364083	0.1725416

REGRESSION DIAGNOSTICS

DIAGNOSTICS FOR HETEROSKEDASTICITY

RANDOM COEFFICIENTS

TEST	DF	VALUE	PROB
Breusch-Pagan test	3	27.96522	0.0000037

DIAGNOSTICS FOR SPATIAL DEPENDENCE

SPATIAL ERROR DEPENDENCE FOR WEIGHT MATRIX : rook.GAL

TEST	DF	VALUE	PROB
Likelihood Ratio Test	1	1.35864	0.2437733

COEFFICIENTS VARIANCE MATRIX

CONSTANT	RURAL	ELEV_DIFF	SOIL_COMB	LAMBDA
4951.429580	-5304.868041	-1.822331	-7127.313772	0.000000
-5304.868041	7337.760583	-1.275694	8283.052469	0.000000
-1.822331	-1.275694	0.009961	-1.339864	0.000000
-7127.313772	8283.052469	-1.339864	24823.423472	0.000000
0.000000	0.000000	0.000000	0.000000	0.037709

OBS	BU_T_100_0	PREDICTED	RESIDUAL	PRED ERROR
1	0.00000	-4.00202	9.05197	4.00202
2	3.10000	28.36635	-23.90905	-25.26635
3	31.10000	19.85594	20.24279	11.24406
4	0.00000	6.51161	-8.20254	-6.51161
5	0.56000	0.82310	-1.01486	-0.26310
6	7.68000	15.58692	-16.52352	-7.90692
7	0.00000	67.68050	-70.78534	-67.68050
8	45.43000	58.29259	-11.06629	-12.86259
9	0.00000	31.27622	-32.59871	-31.27622
10	209.50000	94.73470	121.64492	114.76530
11	125.11000	53.53992	74.68560	71.57008
12	9.73000	52.13107	-35.61207	-42.40107
13	0.00000	-28.86630	26.97115	28.86630
14	63.93000	98.20529	-35.39997	-34.27529
15	59.19000	57.42106	6.25832	1.76894
16	4.08000	72.98844	-56.96094	-68.90844
17	0.00000	24.10460	-31.88353	-24.10460
18	58.91000	66.33252	-13.66306	-7.42252
19	83.75000	60.53804	24.23687	23.21196
20	66.07000	74.97293	-8.30133	-8.90293
21	27.39000	85.07852	-81.91591	-57.68852

22	434.12000	93.17812	330.33394	340.94188
23	8.10000	95.06445	-82.55920	-86.96445
24	8.73000	47.54278	-30.40582	-38.81278
25	82.11000	56.30837	11.18168	25.80163
26	30.02000	42.56819	-40.93654	-12.54819
27	24.74000	-13.30109	18.73022	38.04109
28	3.35000	-13.45330	33.74949	16.80330
29	350.41000	81.63606	256.57758	268.77394
30	6.19000	82.05970	-71.52988	-75.86970
31	70.40000	81.34305	-14.64212	-10.94305
32	0.84000	76.53142	-63.07198	-75.69142
33	8.92000	49.90534	-30.91168	-40.98534
34	87.04000	104.85089	-18.57893	-17.81089
35	65.25000	106.42838	-55.81545	-41.17838
36	51.46000	77.76759	-15.67546	-26.30759
37	38.06000	99.67829	-57.34113	-61.61829
38	45.80000	50.12262	2.27535	-4.32262
39	8.98000	80.87824	-60.42402	-71.89824
40	86.58000	81.87627	7.34753	4.70373
41	45.72000	22.33140	26.85355	23.38860
42	85.38000	88.14779	-0.41164	-2.76779

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